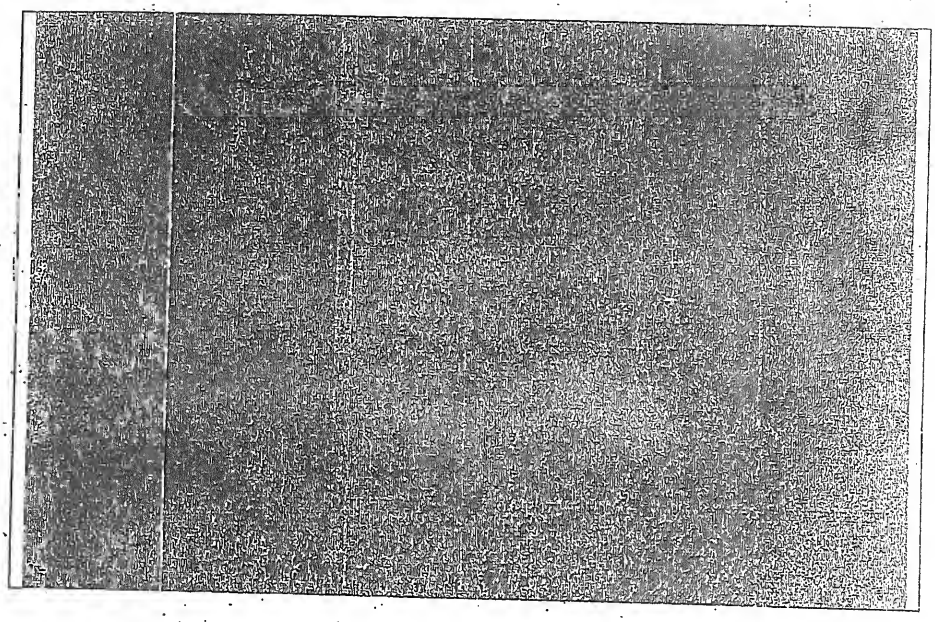


Acne Vulgaris

By
Dr.Hany Abo Elwafa

SG

- Site. All except... maximum sites:
- SG ass. ? H-F Except...
- Type of sec.
- Types of HF acc. to Seb. G.
- (F) → Sebum ?? stimulated of its src.

(F) Structure +/+ &/--

Acne Vulgaris

(Basics)

- Sebaceous Gland (SG) = Pilosebaceous unit = Hair follicle.

A - Embryology: develop at 13-15 th wk. of gestation as Budding from ↓ primordial Follicular epith.

B - Histology:

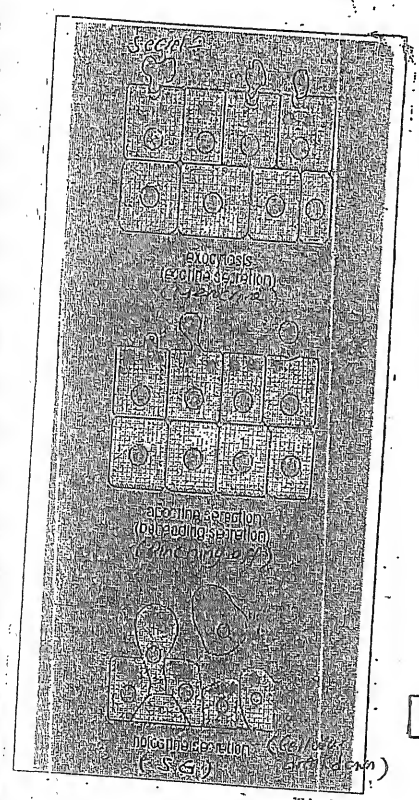
- Holocrine gland: secretion formed by complet destruction of the cells ē Transit time 7-4 d
- ~~xx~~ formed → many lobes each ē a duct (lined by st. sq. epith) → Converge Toward the main Seb. duct → open into the Pilosb. Canal whose Epith. is Continous ē surface Epid. (Infundibulum) space at dossae.

C - Sites: All over the body except < Palms / Soles

- Maximum desity at Sebaceous site (acne sites) = Forehead, Cheeks, upper chest & back (400 - 900 glands / cm^2)
- while other sites 40 / cm^2). ["T-Zone area" of Face.
- In All sites are ass. ē Hair follicles

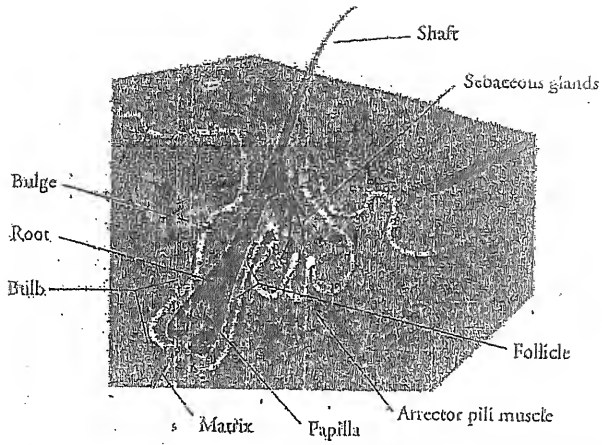
Except: ("sic")

- Meibomian glands: of Eyelids
- Montgomery Tubercles: of Areola.
- TySon's glands of prepuce.
- Fordyce spots at Vermilion boder of lip & mm.

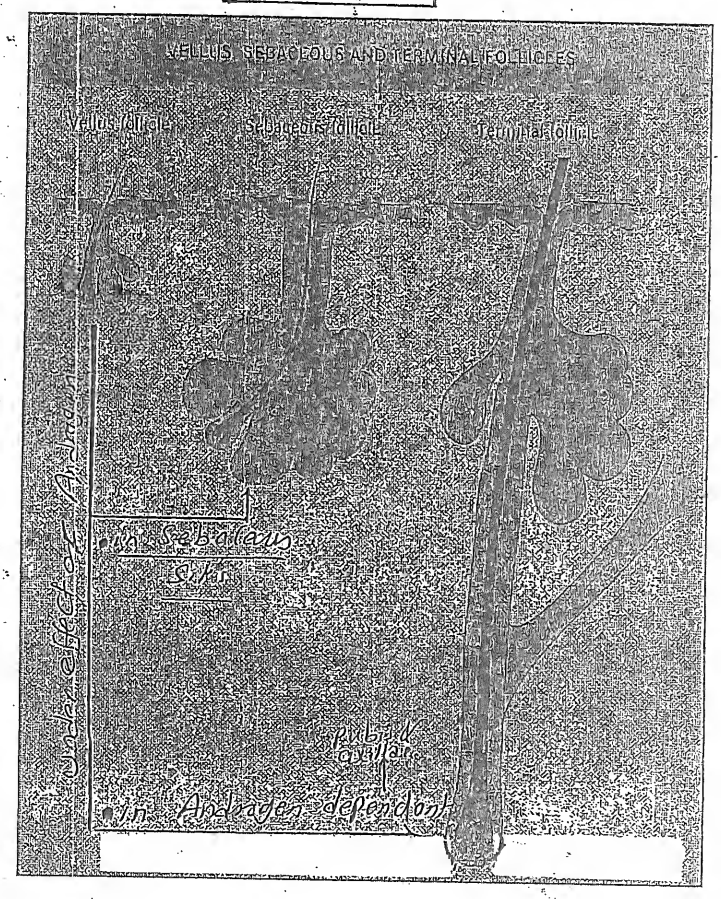


* Types of secretion.

D - Types of SG (pilseb. units):



SG Types

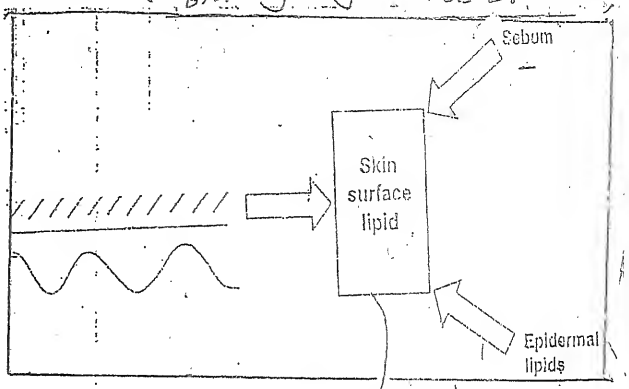


* *Vellus hair follicles:* with a short thin hair and small sebaceous glands
* *Sebaceous follicles:* with a midsized hair and large sebaceous glands; they are seen only in humans, especially on the face and the upper portions of the chest and back (the most common sites of acne vulgaris)
* *Terminal hair follicles:* with a long thick hair and fairly large sebaceous glands

Sebum Biochemistry

- Complex mixture of lipids that is secreted from the sebaceous glands.

- Sebum + Epid. lipids = Skin surface lipids (after Hydrolysis TGs by Lipases)
  - Sebum: TGs, cholesterol, cholest. Esters, wax esters, squalene
  - Epid. lipids (from Epid. keratinizate) as sebum
    - But No: Squalene, wax esters & much < TG, Chol.



- NB: Wax Esters & squalene: are unique to seb. gland of Humans also, not present in Epid. lipids & in lipids of internal organs
- (X) Squalene: in other tissues (Epid. & internal organs) → rapidly converted to sterols (cholesterol)
- So, wax Esters & squalene are unique to S.G & To Human.

- as Sebum: But there are FFAs (formed by effect of lipolytic enzs present in sebaceous ducts on TGs.

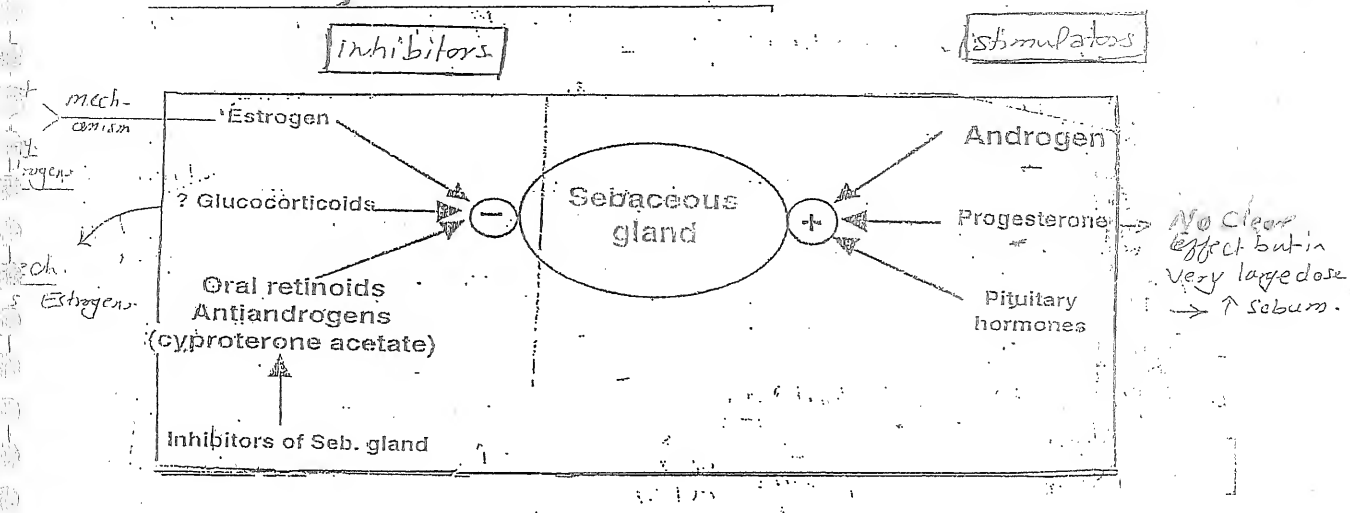
Test:
- ⊙ S.G < Squalene / Wax esters
- ⊙ Epid. lipids: High conc. of TG / Chol.
- ⊙ Skin surface lipids: FFAs.

- Measurement of sebaceous activity
  By placing a pad of cigarette papers for 3 hrs. on a limited area of forehead and then the sebum is extracted with diethyl ether.

Function of Sebum:
1. Moisturizer (↓ Epid. water loss).
2. protective (d.t FFAs): against < Bacteria / Fungi (so T. Capitis Rare after Puberty)
3. Contain Vit E → antioxidant.

"C in"

1. Control of Sebum Secretion (Endocrinal control)



- Androgen is the Main Stimulator for SG secretion

↓ so

- This the Cause of Hyperandrogenic Cut. diseases or SAHA synd.
(Seborrhea, ACne, Hirsutism & AGA)

- Basics of Androgen secretion & Metabolism
(Hirsutism أضف)

- in Men Source of Androgen — Adrenal gland / Testes.
- in ♀ " " " — Adrenal glands, ovaries.

- SG Contains 3 enzymes:
  - 3 β HSD (3β Hydroxy steroid dehydrogenase)
  - 17 β HSD
  - 5 α reductase (II → all ducts & I → all gland lobes)

- at Adrenarche (7-10 y) → ↑ DHEA-S $\xrightarrow{3\beta HSD}$ → Androstenedione $\xrightarrow{17\beta HSD}$ Testosterone $\xrightarrow{5\alpha\text{ reductase}}$ (I)

DHT. (أقوى من T) → affect KCs & Sebocytes.

Acne Vulgaris

- **Def:** Chr., inflammatory disorder of pilosebaceous unit
- **Cl- By formation of** → Comedones (Dry lesions).
  papules / pustules
  nodules / cysts
  ± scarring

Epidemiology

- **Incid:** 50% of Both Sexes.
- **onset:** Generally 15–18 Ys (< Boys: 16–19; Girls: 14–16 Ys); However Late onset ± Present 20–35 Y (women)
- **Resolve:** at mid twenties (usually < 25 Ys; However,
  : 12% of women
  : 8% of men
  ] may still have acne thro 45 Ys

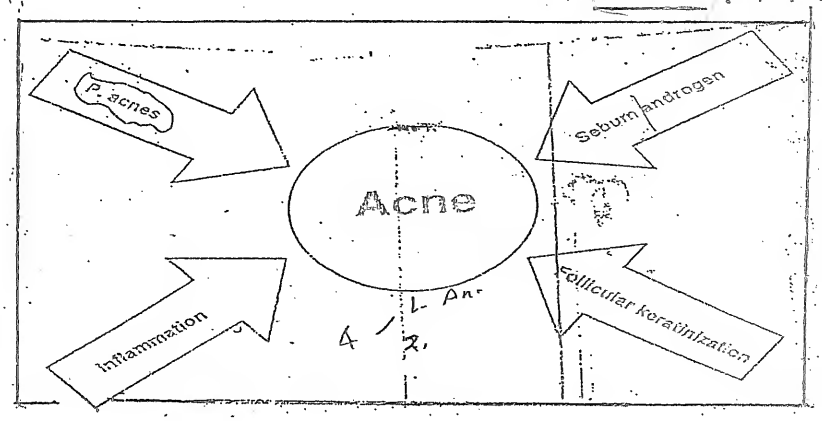
Pathogenesis

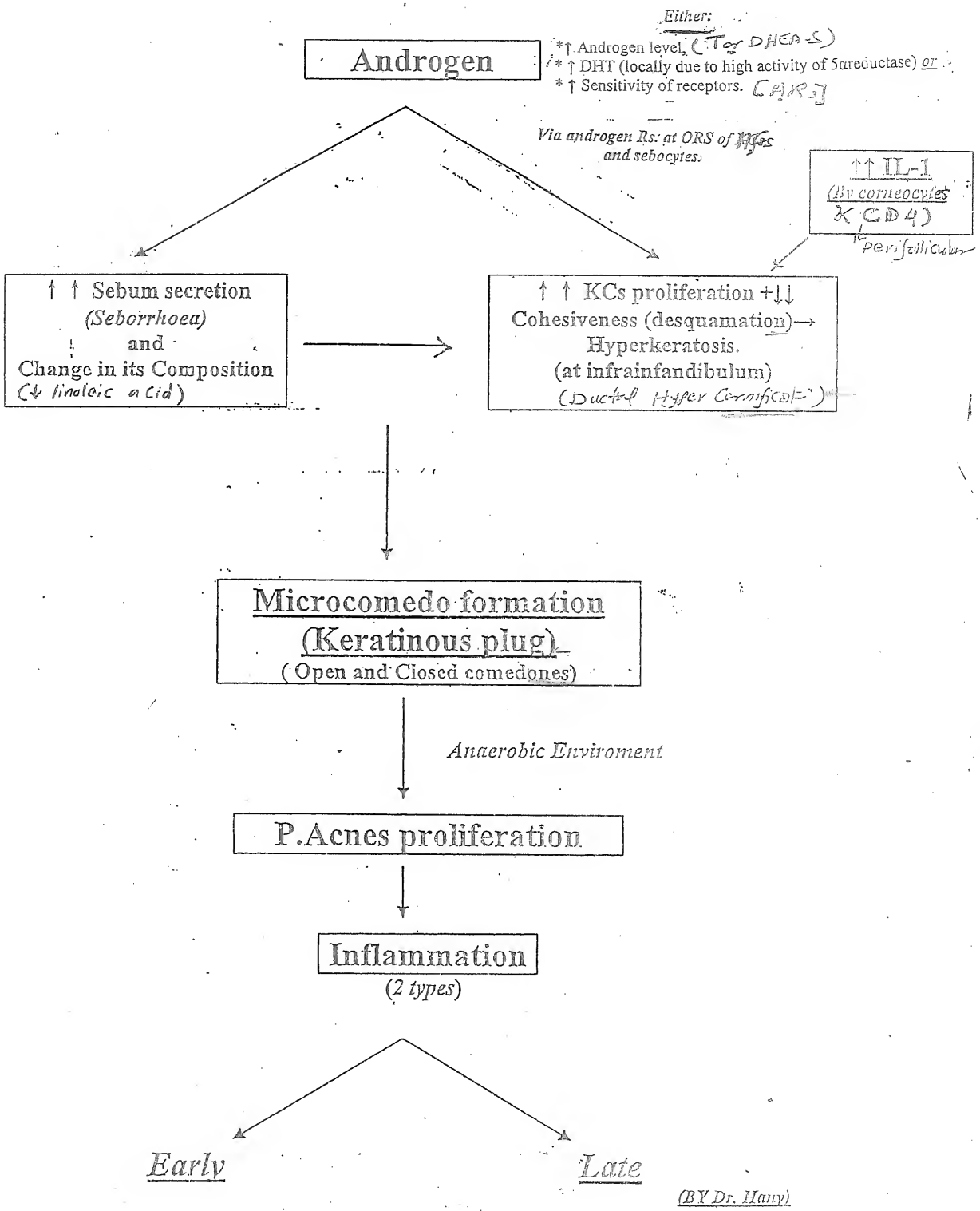
* 4 Key Factors:

1. ↑ Sebum (Seborrhea)
2. Ductal Hyperkeratinization & Microcomedo formation.
3. P. Acnes, proliferate.
4. Inflammation.

* other Factors:

- **Genetic:** +ve FH often present but definitive genetic data still lacking
- **Diet** (ADS): Controversy but Recently: Hyperglycemic diet & milk & Junk food.
- **Premenstrual Flare:** 2–7 ds before Menses either d.t (↑ progest.) or d.t hydrat. of piloseb. unit.
- **UVR:** may improve or Exacerbate acne (d.t ↑ Comedogenicity of Sebum)
- **Stress:** ↑ Acne (d.t substance P)




Either:
Androgen
*↑ Androgen level, (↑ of DHEA-S)
* ↑ DHT (locally due to high activity of 5αreductase) or
* ↑ Sensitivity of receptors. (AR)
Via androgen Rs: at ORS of hfs and sebocytes.
↑↑ IL-1
(By corneocytes & CD4)
Perifollicular
↑ ↑ Sebum secretion
(Seborrhoea)
and
Change in its Composition
(↓ linoleic acid)
↑ ↑ KCs proliferation +↓↓
Cohesiveness (desquamation)→
Hyperkeratosis.
(at infrainfandibulum)
(Ductal Hyperkeratinization)
Microcomedo formation
(Keratinous plug)
(Open and Closed comedones)
Anaerobic Enviroment
P.Acnes proliferation
Inflammation
(2 types)
Early
Late

(BY Dr. Hany)

NBs on pathogenesis

(1) Hyperandrogenic cut. diseases may occur d.t:

1. ↑ Test. or DHEA-S levels (rare).
2. ↑ DHT d.t ↑ local activity of Enz. 5α reductase
3. ↑ Sensitivity of Androgen Receptors to / NL Circulating levels of Testosterone or DHT.

(End organ responsible path.)

(2) Propionibacterium (Corynebacterium) Acnes:

- NL inhabitant of infundibulum (lower part).
- Anaerobic / Microaerophilic, Gram +ve rods.
- Produce Coproporphyrin III So:
  - show red fluorescence by W.L
  - Can be Targeted by laser/light.
- Types:
  - ① P. Acnes (commonest)
  - ② P. Parvum
  - ③ P. granulosum
  - ④ P. avidum
  - ⑤ Propionicum.
- other diseases produced by Propionebacteria (see bact. Rf.)
- other diseases produced by P. Acnes:
  - AV
  - Progressive Macular Hypomelanosis
  - Dental Inf.
  - Endocarditis
  - Conjunctivitis & Keratitis
  - brain abscess.
  - osteomyelitis.

- Acne Miliaris
- Perioral dermatitis.

HL:

Propionibacterium species are inhabitants of the skin and are usually nonpathogenic. As a result, they are common contaminants of blood and body-fluid cultures. These species are slow-growing, nonsporulating, gram-positive anaerobic bacilli and require at least 6 days for growth in culture.1 Propionibacterium species belong to the genera of coryneforms and are the best studied because of their association with acne vulgaris. found briefly on the skin of neonates, but true colonization begins during the 1-3 years prior to sexual maturity. During this time, numbers of P acnes rise from fewer than 10/cm2 to about 106/cm2, chiefly on the face and upper thorax. In the lipid-rich icroenvironment of the hair follicle, P acnes produces inflammatory mediators that result in papules, pustules, and later, nodulocystic lesions that are typical of inflammatory acne.

NB : organisms involved in AV (inhabitants of Hair follicle):

① Malassezia (at upper or acr. infundib.).
② Staph. Epidermidis (at med. infundib.). (MSP)
③ P. acnes (at lower N).

(3) Inflammation: There are 2 Types of Inflamm. in AV.

even before Hyperkeratinization

→ Early (before rupture of ! Comedo) d.t:

A. in Acne sites of genetically predisposed individuals, there are Perifollicular Presence of CD4 (T helper).
That → IL1α →
follicular Hyperkeratinization & Microcomedo formation.

B Chemotactic factors:

- P. Acnes → ++ Toll like receptor 2 (TLR2) on surface of Monocytes, Macrophages & PMNL → Chemotactic factors as:
  - IL1-α
  - IL8
  - TNF-α
  - PG like
  - ROS (by PMNL)

→ Early Inflamm.

أول خلايا بتيجي هي Lymphocytes

Late (d.t rupture of ! Comedo).

↓

d.t this (P. Acnes) That produce:

Enzymes as:

- proteases
- Hyaluronidases
- lipases (Use act on Sebum → ↑ FFa → ↑ KCs prolif.)

↓ digestion of Walls of Comedones

↓ liberation of their contents (Sebum, Keratin & bact.)

↓ FB reac. →

Inflammat.

↑ ↑

(Papules Pustules Nodules Cysts)

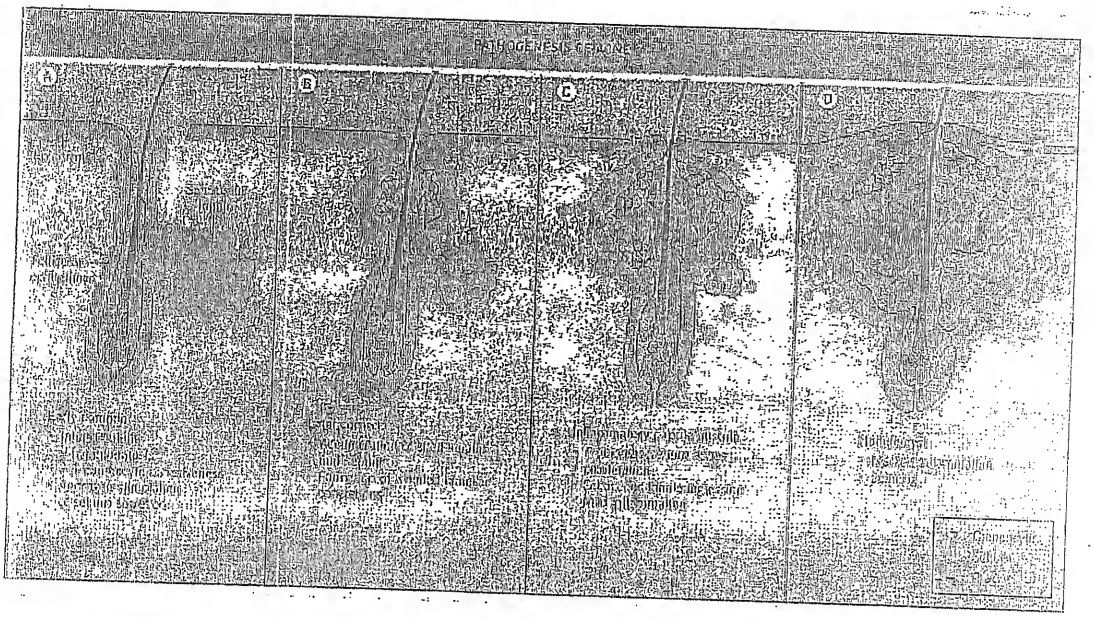
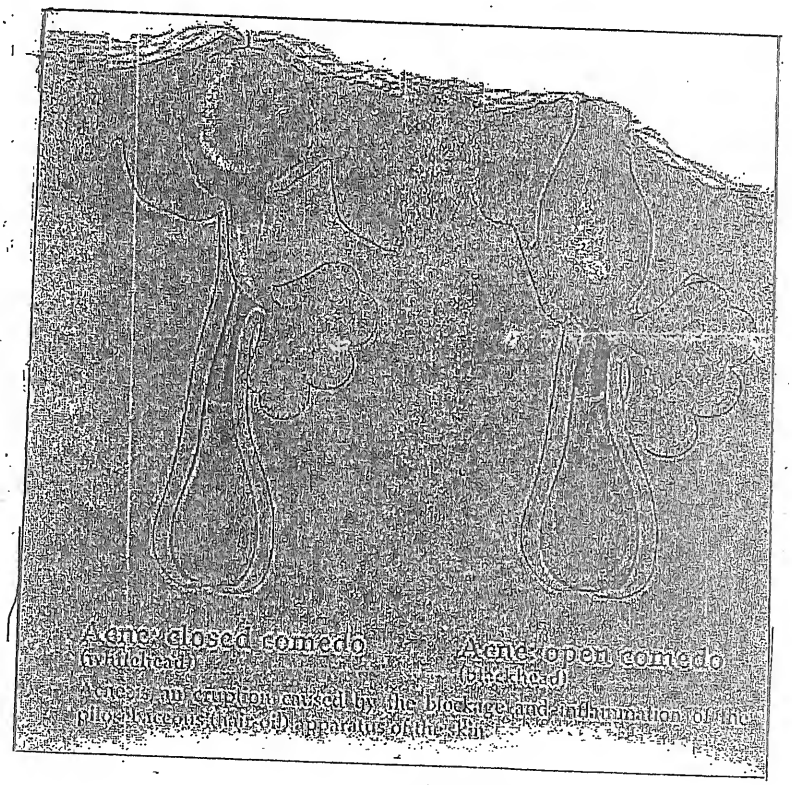


Fig. 37.1 Pathogenesis of acne.



CIP of AV

Classical AV

CIP
Grading

- lesions can be classified into:

1-Non-inflammatory lesions: (dry lesions).
Open comedones (blackheads)
Closed comedones (whiteheads)
Uninflamed nodules (sometimes called cysts)
2-Inflammatory lesions: Papules, Pustules and Inflamed nodules.
3-Secondary lesions: excoriations, erythema and hyperpigmentation, scarring.

- N.B Comedones are dry lesions of Acne ... can be classified Acc. to

Size

1. Micro (not seen clinically)
2. Macro > 1 mm.

Level of obstruction

Open Comedones (Black heads)

- obst. is superficial
- Pore: Partially blocked & communicate ē skin surface → Sebum oxidation → black discoloration (also + d.t. ↑ Melanin & not d.t dirtiness).
- dont progress to inflamm. lesions
- Easily Treated.

Closed Comedones (White head)

- obst. is deep
- Pore: is completely blocked dont communicate ē skin surface → No Sebum oxidation → No. black discoloration
- progress to inflamm. lesion.
- difficult to be treated.

- Site: Face (Forehead, cheeks, ± Nose, Ear (Comedones)), upper Chest & back, upper arm.

Acne Grading (No universally Accepted Method)

Easy Method (one)

1. Mild → Comedones ± Papules
2. Mod → as mild + Papules + pustules.
3. Severe → as mod. + Nodules & Cysts.

Variants [Acneiforms Eruptions]

- Acne Conglobata
- Acne Fulminans
- G-ve Folliculitis
- Neonatal Acne
- Infantile Acne
- Acne Mechanica
- Acne Excoriée ....
- Occupational Acne
- Chloracne.
- Drug induced Acne.
- Acneiform Eruptions.

B). 2nd Classification: "Combined Acne Severity Classification."

Combined acne severity classification Severity	Definition	
Mild acne	Fewer than 20 comedones, or Fewer than 15 inflammatory lesions, or Total lesion count fewer than 30 C<20,<15,<30)	<20 <15, 30
Moderate acne	20–100 comedones, or 15–50 inflammatory lesions, or total lesion count 30–125	
Severe acne	More than 5 nodules, or Total inflammatory count greater than 50, or Total lesion count greater than 125	>5 >50 >125

NB: Population-based and migration studies have suggested a correlation between diet and acne. Large, well-controlled, observational studies have demonstrated that diets high in dairy products are associated with an increase in the risk for and severity of acne. Researchers have found significant associations between all varieties of cow's milk and acne. The relationship between milk and acne severity may be explained by the presence in dairy of normal reproductive steroid hormones or the enhanced production of polypeptide hormones such as IGF-1, which can increase androgen exposure, and thus, acne risk. Recent findings also describe an association between a high-glycemic-index diet and longer acne duration. In addition, randomized clinical trials have demonstrated that a low-glycemic-load diet can influence hormonal levels and improve insulin sensitivity and acne. No study has established a positive association between acne and chocolate, saturated fat, or salt intake. [Skin therapy letter; 2012]

Also: Acne ↑ c̄ Junke Foods (الشيبسي. الكولا)

Treatment of Acne

1. General Measures.
2. Specific Measure.
3. Ht of compliations.

A. Patient Education:

- AV is a physiological process that Needs prolonged & mentainance ht as long as it is present
- ht is for Control, Not for Cure (Except ē Isotretenoin)

- No improvement in AV before 6-8 wks.
- Avoid milk, Emotional stress (Squeezing of lesions)

B. Causes of ht failure: (2C, 2D)

- Bad compliance. (Commonest)
- Drug Interactions. "AV"
- Drug resistance.
- Coexisting underlying problem. e.g. Suprarenal Fm, PCOS

C. Assesment Acne Severity: By assesing AV

- Type (mild-med.-severe)
- Psychological condition
- degree of scarring

2. Specific Measures:

A. Medical ht:

علاج الاعراض أو
علاج سبب الـ AV

1. Remove the plug — BY → "Comedolytic"
2. -- of P. Acnes → Antibiotics
3. ↓↓ Sebum → BY < Hormonal or Non H
4. Anti-inflammatory → BY: Adapalene, Azelaic acid, Antibiotics, Isotretenoin.

1. Comedolytics
Keratolytic
Plug
Salicylic acid
Sulfur
Resorcinol
Retinoic acid derivatives:
(Topical retinoid)
Tretinoin (Retin A)®
Adapalene (Differin)®
Tazarotene (Zanlex)®
Isotretinoin (Isotrex)®
(±) Azelaic acid (Skinoren)®
Benzoyl Peroxide 5% (Panoxyl 5 gel)
(BP)
P.Acnes
Inhibition BY
2. Antibiotics
Topical
Erythromycin
Clindamycin
Benzoyl peroxide (BP)
Azelaic acid
Systemic
Tetracycline
Doxycycline
Minocycline
Erythromycin
Azithromycin
Clindamycin
TMP+SMX (Septrin)®
Sebum
3. ↓ Sebum
BY:
Hormonal
Non Hormonal
Isotretinoin
BY
Anti-Androgens
Cyproterone acetate
Spironolactone
Cimetidin.
Androgen inhibitors
low dose dexamethasone
OCPs
GnRH analogs
Finasteride
Dutasteride.
The following drugs have double Act:
1- B.P < Antibacterial (++) mainly
Comedolytic (+)
2- Azelaic: antibact. & Comedolytic

• أول كورس

Remove the plug By comedolytic.

1. Comedolytics

• salicylic acid, sulfur & Resorcinol : old Comedolytics, not used commonly nowdays.

• Retinoids (Synthetic analogues of Retinoic acid)

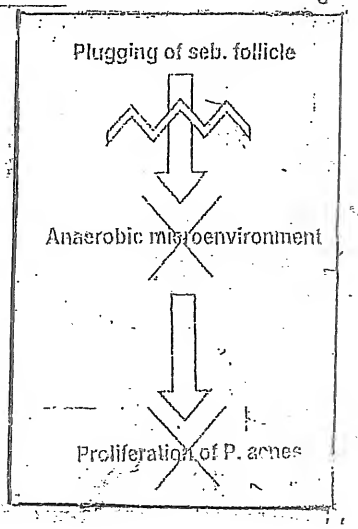
A. Tretinoin (0.1%, 0.05% & 0.025%) → have 2 types of Receptors (for details see section of Retinoids).

- Cytoplasmic
  - CRABP (Cellular Retinoic acid Binding protein)
- Nuclear
  - RAR (Retinoid acid receptors)
  - RXR Retinoic X Receptors.

* Retinoids + CRABP —(Carry them to Nuc.)→ bind to Nuclear Receptors on DNA → affecting differential gene expression

• Mechanism:

1. Comedolytic → Treat already present Comedones (by) Normalization of follicular Keratinization & ↓ cohesiveness of abnl follic epith.
   → Prevent new Comedo formation
2. Anti-inflammatory: -- leukocytes activity, -- Cytokines release & -- Toll Like Rs.
3. Facilitates penetration of other drugs.



معنى كلام
لازم نركب
بدون
Retinoids.

S.E

1. Irritation (CD) to avoid:
   - start ē cream base (لا يجب ... gel & sol.)
   - M ē lower concentration (0.025% → ↑)
   - gradually ↑↑ application period.
   - gradually (↓↓) application interval
   - completely dry skin.

(تشنيف الجلد بالساعة ينشفه بعد الغسيل)
تجنب الصابون & إستعمال ...

(stepwise increment done every 3-4 wks)

2. Photo irritation:
   - apply at night & ↓ light exposure.
   - wash at morning & use sunscreen.

1. Toxic photo-irritation
2. To its degradation
→ "photo-labile"

3. pregnancy & Lactation: Category (C) so avoid it during ♀ (for medicolegal)

4. Acne exacerbation: during 1st (4 wks)
   exacerbation may occur d.t externalization of deep seated lesions.

Instructions:

1. دهان مساء كل يوم طبقة خفيفة مع عدم التعرض للضوء
2. تنشيف صباحاً قبل الخروج ووضع عازل شمس
3. ممنوع الدهان في ٣ مناطق
   - حول العين
   - زوايا الفم
   - Nasolabial fold.
   → Irritation → Hyperpigm
4. مفيش نتيجة الا بعد: ٦-٨ أسابيع
   أفضل نتيجة بعد: ٣-٤ شهور
   ... عليه باستمرار.

(ملاحظة: صابون ماء ...)

NB. if cream base is not effective → use sol. or gel form (more effective)
- after a period of cream base use → shift to sol. or gel.

- Total absence of skin irritation should lead the physician to suspect that topical therapy is not being used correctly!!
- Transient stinging is a useful sign of adequate coverage.

- **Adapalene 0.1% gel** : differs from (Retin A®) in: (13)
  - doesn't bind to CRABP but bind to the Nuclear receptors specially RAR β & RAR γ.
  - More effective > 0.025% Tretinoin gel.
  - Less irritant → well Tolerated
  - Light stable → Can be used at morning
  - More potent antinflammatory effect (double Act)
- **Tazarotene 0.1%** : may be used daily or short contact Therapy
  - Selectively binds to RAR γ & Not RXR.

NB :
- Retin A & Adapelene → Category "C" in Pregnancy
- Tazarotene & Isotretinoin → Category "X".

Topical Antibiotics

2- inhibit of P. Acnes BY Anti-biotics

- Erythromycin
- Clindamycin
- (BP) Benzoyl Peroxide 5% → Antimicrobial + antinflamm.
- Azelaic acid → " + comedolytic

- **Erythromycin & Clindamycin** :

(1) applied to the affected area Not to the lesion because the peripheral zone of the lesion will receive sub-therapeutic concentration → bact. resistance.

(2) should be used + Zinc or BP → ↓ Bact. Resistance

Erythromycin 4% / Zinc acetate 1.2%

(Zincomycin, Acne-Benz / Acne-Zinc / Acnidu C) → BP + Erythromycin

(B)
- B.P & Azelaic → No Resistance.
- Erythromycin + { Zinc : Zincomycin (Acnezinc) lot ® ; BP : Acnebenz gel. ® }

(3) Should be the same type of systemic antibiotic e.g. avoid dissimilar antibiotics.

- **Benzoyl peroxide 5%** : (Panoxyl 5 gel)®
  - double mechanism of Action (see before)
  - عالمية
  - 2.5% – 20%
  - Antimicrobial: Bactriostatic d.t liberation of free O.
  - Comedolytics & TG Hydrolysis
  - S.E
    1. irritation
    2. Bleaching of clothes & Hair (المخدة - الملابس الشعر)

دهان موجود بعد
- **AZelaic acid** (20%) (Skinoren, Ezalic)®
  - Def. → Naturally occuring dicarboxylic acid that derived from [P. ovale = Malassezia furfur]
  - مفيد علاج: 1- الكبر علاقية 2- تفتيح لبقع مكان ضعيف
  - Mechanism: (No effect on sebum).
    - Acne →
      - Comedolytic
      - Antimicrobial
      - Antinflammatory (↓ ROS release from Neutrophils)
    - Pigmentary disorders → Bleaching Effect (↓ Pigm.): affect the Hyperactive MCs not the NL.
    - MM (Malignant Melanoma) → Arrest MM progression.

Systemic Antibiotics

1. Tetracyclines
2. Erythromycin
3. AZithromycin
4. Clindamycin
5. TMP + SMX

Tetracyclines

(تحريري - شفهي)
(Comprehensive 2010).

Classification:

Short acting (half life: 6-12 hrs)
- Tetracycline
- oxytetracycline.

Intermediate acting. (16 hrs)
- Demeclocycline
- Lymecycline.

long acting (18-22 hrs)
1. Doxycycline
   - Hydrate
   - Monohydrate (Granudoxy tab)®
2. Minocycline
   - Minocycline
   - Minocycline HCL

Mechanism of Action:

Antibiotic Mechanism

Bacteriostatic by -- bacterial protein synthesis Through binding to "30S" subunit of bacterial ribosome.

So Active against:
1. G+ve (staph & strept)
2. G-ve (but < G+ve).
3. others:
   - P. Acnes
   - Mycoplasma
   - chlamydia.
   - Rickettsia
   - spirochaetes
   - some Parasites.

Non antibiotic Mechanisms

1. Antiinflammatory: inhibit Neut. & Eos. chemotaxis
2. Anti metalloproteinases: (Enz. that -- Collagen & gelatin products). → Cs ↓ scarring
   (Anti Collagenolytic effects)
3. ↓↓ Angiogenesis.
4. ↓↓ Apoptosis.

Ess Tetracyclines in acne act By:
1. ↓ P. Acnes → ↓ inflamm.
2. direct (intrinsic) antiinflammatory.

(Antibacterial & Antiinflamm.)

Pharmacokinetics:

(1.) Absorption:

- Tetracycline → لازم تتاخد على معدة فاضية ليه ؟؟
  - its abs. impaired (chelates) by:
    - منتجات الالبان dairy products
    - (in Antacids) → Alum. hydroxide
      - Ca+ · Zn · Fe
      - bisthmus subsaligylate.
- ممكن تؤخذ بعد الأكل · Doxy & Mino. → لا علاقة لهما بالأكل

(2.) Half life:

- Tetracycline → 6-12 hrs. (short acting).
- Demeclocycline → 16 hrs. (intermed. ").
- Doxy & Mino. → 18-22 hrs. (long ").

(3.) Excretion:

- Via Kidney Except Doxy. (via GIT)
- So CRF → prolongs half life & Doxy. is the Safest with CRF.

N.B. Tetracyclines are lipophylic & reach higher concentrations in nails & skin.

Indications (Dermatologic):

also used in Ttt. of:
- Urethra · pelvis
- chest

Common indications (Anti-P. acnes)

- FDA approved
  - AV (Minocyc. HCL for ttt of inflamm. non nodular acne in Pt > 12 ys)
- Non FDA app.
  - (a) Rosacea.
  - (b) Perioral dermatitis.
  - (c) Hidradenitis.

less common indications

- "Bullous diseases" → Tetracycline + Nicotinamide for ttt of:
  - PV
  - B.P
  - CP
  - DH
- AIDs related KS
- pruritic pigment.

أشهر
S.E

1. Tetracycline < GIT / candidiasis
2. Doxy → photosensitivity & onycholysis.
3. Minocyclin → Syndromes + Pigmentat
   - . Skin
   - . MM
   - . teeth
   - . Nail
   - . S Ca
   - . Generalized
4. Erythromycin: → GIT
   → -- CYP 450
5. Clindamycin: Pseudomembranous Colitis.
6. TMP+SMX: STS.

Tetracyclin
1-2 gm/d

1-2 gm/d

Doxy or Mino - 50-200/d mg

Doxy: 20 is subantimicrobial dose (-- inflamm but not bact. So No resistance).

Minocyclin
الأقوى
Resist أقل
S.E أكثر

S.E of Tetracyclines:

(1) GIT effects: → to ↓ it take ē food (non diary products). [Doxy & Mino not Tetra]

- Nusea
- Vomiting
- Epigastric burning.
- Abd. discomfort.
- Pancreatitis & Esophagitis. → علشان كده لازم كوباية مية كاملة
- Hepatotoxicity (sp. in large doses & in pregnant).

(2) Renal: Fanconi's synd & progression of uremia in patients ē renal dis.

لو منتهي الصلاحية لازم تحرص على الصلاحية → Fanconi's

(3) Vestibular toxicity.

(4) Phototoxicity & onycholysis: (sp. Doxy & Demeclocycline).

(5) Gram -ve folliculitis (after prolonged intake).

(6) Children < 9-12 ys: "brown" discoloration of bone & Teeth & GR of bone. [permanent] "also Enamel Hypoplasia"

(7) Minocycline: ← خطير علشان كده لا تقصر استعماله على الرغم انها نادرة.

- SJS
- Sweet's Synd.
- depersonalization Synd.
- DRESS drug Hypersensitivity synd. (Fever, rash, LN & MOF). (Hyperpigm)
- L.E.
- Serum sickness like reaction. (...)

(8) Other S.E:

- Minocycline → Blue-black Hyperpigm. of skin, Nail, Teeth, Tongue, sclera.
- Flaring up of Candidal Vaginitis.
- Gynecomastia.
- Pseudotumor Cerebri (if + Isot.)
- Phlebitis (if IV)
- leukocytosis, atypical lymphocytes & ↓ PPlat.
- Neuromuscular blockade. (S- in MG).
- Demeclocycline → Diabetes in Gl dis

- Contraindications:
  - pregnancy (Category D)
  - lactat^ (not safe).
  - Children < 9-12 y: (??)
  - Liver & renal impairment.
  - With iron, Ca, & dairy products of Antacids.
  - at bed time → Eosophagitis.
- Interactions: they:
  - ↑↑ Effect of → oral anticoagulants, Digoxin & Insulin.
  - ↓↓ " of → OCPs. [oral Contraceptives]
  - + Isotretinoin → (Pseudo tumor cerebri)
  - CYP450 Inducer. (Cytochrome P 450)
- Dose:

Patients differ in the amount of tetracycline they need to control inflammatory skin diseases. A full daily dose of tetracycline is generally prescribed for the first few weeks or months to see how well it controls the skin problem. This full dose should be continued for most patients with acne. However, those with rosacea and perioral dermatitis may be able to reduce their dose at approximately monthly intervals.

- Tetracycline: 250-500mg four times daily (1-2 gm daily)
- Oxytetracycline: 250-500mg four times daily
- Demeclocycline: 150-300mg twice daily
- Doxycycline: 50-100mg once or twice daily (50-200 /d)
- Lymecycline: 300-600mg once or twice daily
- Minocycline: 50-100mg once or twice daily (50-200 /d)

There's a lag period of one to three weeks between the change in dosage and its effect on skin. If the skin problem becomes worse, return to the previous higher dosage and continue on it or as advised by your doctor.

Precautions

- TMP+SMX → Regular Strength: Backrim — SMX 400 mg / TMP 80 mg
  → DS = Septrin = 800 mg + 160 mg.

- Dose in Children — 40 mg/kg/d SMX
  8 mg/kg/d TMP

(2) ErythromyCin: → (Main use in pregnant)

- Dose: 1 gm/d (250–500 /1–4 hours)
- S.E: GIT upset & ↓Cyp 450.

(3) AZithromyCin:

- ✓ Dose: • كبسولة (٥٠٠) يومياً لمدة ٣ أيام
ثم راحة ٤ أيام [غالباً كل جمعة] لمدة شهر.
(على معدة فاضية)

(4) ClindamyCin:

- Dose: 300–450 mg/d
- S.E: Pseudomembranous Colitis. →
  - def.: Inf. of Colon BY Clostridium difficile ↓ d.t. flora affection
  - manifs: Abd. pain, diarrhea, fever, Toxic Mega-Colon ↓ ttt: Vancomycin, Flagyl.

(5) TMP (160) + SMX (800) (Septrine DS).

- Dose: 400–600 mg/d
- S.E: • BM ↓ ↓
  - drug Eruption ↙ "SJS/TEN" (So of limited use).
  - pregnancy (D)
- NB: Main use in Dermatology: G-ve folliculitis ↓ (تعطيها لما [illegible])

فترة العلاج ٣-٦ شهور ولو معنيش نتيجة بعد ٣ شهور ← يوقف

Hormonal ttt of Acne ← (للإناث فقط)

↓ Sebum BY ← Hormonal & non Hormonal ttt.

(Antiandrogens & Androgen inhibitors)

Indications

- Patients ē (Severe resistant Acne) that's not Candidate for (Iso-tretinoin).
- Clues of Hormonal influence →
  - * Adult onset acne. [late onset]
  - * Chr. Inflammatory acne (Painful, deep seated Nodules). ↳ "No Comedones".
  - premenstrual flare
  - distributed at ← Lower face, Jaw line, Chin.
  - Excessive facial oilness (تكبر مسامية)
  - Ass. other Androgenic manifs. (Hirsutism, AGA).

Antiandrogens & Androgen inhibitors

Androgen inhibitors

Inhibit Androgen production By:

- -- DHEA & -- T. products By
  - -- Supra-renal gland
    - low dose Dexamethasone 0.5 mg
    - Ketoconazole.
  - -- Ovaries
    - CPs
    - GnRH analogs.
- -- of DHT products By
  - -- 5α reductase enz.
    - Finasteride (-- Type II)
    - Dutasteride (-- Type I & II)

Anti-androgens

Block Androgen Receptors:

- Spironolactone
- Cyproterone acetate
- Flutamide
- progestrone
- Cimetidine

- Indications of Antiandrogens & And. inhibitors in Dermatology: (Disorders ē Excess Androgens)
  - Seborrhoea
  - AV
  - Hirsutism
  - AGA (androgenic Alopecia)
  - Hidradenitis Suppurativa.

SAHA Synd (Dermatologic androgeni-zation Synds).

---

1. Spironolactone (Aldactone)®

- Mechanism
  - Main: -- ARs.
  - other: -- Androgen Synthesis (by -- ovarian & adrenal CYP 450) Also -- 5α reductase
- Pharmacology:
  - peak level: 2-4 hrs
  - Bioavailability: 90% (after oral)
  - protein binding: 98%
  - Half life: 10-35 hrs
  - Metabolism: to active metabolite (Canrenone)

Antiandrogens & Androgen inhibitors

Androgen inhibitors — inhibit Androgen production BY:

- -- DHEA & -- T. production BY
  - -- Supra-renal gland
    - low dose dexamethasone 0.5 mg
    - Ketoconazole.
  - -- Ovaries
    - CPs
    - GnRH analogs.
- -- of DHT production BY
  - -- 5α reductase enz.
    - Finasteride (-- Type II)
    - Dutasteride (-- Type I & II)

Anti-androgens

- Block Androgen Receptors:
  - Spironolactone
  - Cyproterone acetate
  - Flutamide
  - progestrone
  - Cimetidine

- Indications of Antiandrogens & And. inhibitors in Dermatology: (Disorders ē Excess Androgens)
  - Seborrhoea
    - AV
    - Hirsutism
    - AGA (androgenic Alopecia)
  - Hidradenitis suppurativa.

SAHA Synd (Dermatologic androgenization Synds).

---

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  - peak level: 2-4 hrs
  - Bioavailability: 90% (after oral)
  - protein binding: 98%
  - Half life: 10-35 hrs
  - Metabolism: to active metabolite (Canrenone)

• Indications, C.I, pregnancy: → الجدول 424

Box 23-3: Spironolactone Indications and Contraindications

FDA-approved dermatologic indications
(None specific to dermatology)

Other dermatologic uses (SAHA)
Hirsutism[16–26,34,35]
Acne vulgaris[27–31]
Androgenetic alopecia[32,33]
Hidradenitis suppurativa

Contraindications
Renal insufficiency—acute or chronic
Anuria
Hyperkalemia
Pregnancy
Abnormal uterine bleeding (AUB)
Family or personal history of estrogen-dependent malignancy*

Pregnancy prescribing status—category (C)

* This would include breast, ovarian, or uterine malignancies.

S.E (A) as All antiandrogens has 2 Common S.E.

- GIT
- ♂ – ??
- ♀ ←

1. Irregular Menestruat° (AUB)
2. Feminizat° of ♂ Fetus if given during pregnancy. → to avoid this → give OCPs.

How to avoid?? [it may resolve ē in 2-3 m of Rx].

- ↓ dose (50–75 mg/d)
- adding OCPs
- Cycling dose: مع بعض أشوكر زي الـ OCPs يعني ياخد ٢١ يوم

(B) Hyperkalemia: "نادرة"

- Serious & most likely to occur in Pt. ē renal insufficiency.

(C) Gynecomastia. (in ♂)

(D) Estrogen dependant Mg e.g Controversy

(E) GIT Symptoms.

- **Monitoring:**
  1. K. level — خصوصاً مرضى الكلى
  2. B.P
  3. Wt.

* - **Drug interactions:** (small list)
  - دواء للضغط (K^+ + ACE-I) — With (ACEI) & K^+ ⟶ Hyperkalemia
  - With Salicylates ⟶ ↓ diuretic effect.
  - With Digitalis ⟶ ↑ level of it

- **Dosage & Form:**

2 Forms

Oral	Topical
في السعودية tab: 25, 100 mg	٥٪ الكتروني للسبيرونولاكتون
dose in Adu: 50 - 200 mg	خارجياً
مع الأكل	. تستخدم في علاج حب الشباب
يومياً أو ٥٠ يومياً في الشهر	لتقليل Sebum :
	. لا توجد دراسات كافية عنه .

- **Efficacy**: in tt of Hirsutism it is
  - potent > Finasteride &
  - less potent < Flutamide.

---

2. Cyproterone Acetate:

- progestin derivative
- Mech.
  - Main: Antiandrogen. [-- ARs].
  - Other: Strong progestional Activity (-- FSH & LH)
- Indications:
  - FDA
    - BPH
    - Cancer prostate.
    - ↓ libido in sexual deviated behaviour.
  - off label
    - See table of dermatologic indication.

• Forms & Dosage: Cypraterone acetate present either

Alone (Androcure 10 & 50 tab) ©
مسرحي كاسي للمدة ١٤ يوم

or

Combined e EE why??
(Diane 35 & 50 tab)
[2mg Cyp. + EE < 35 Mg or 50 Mg.]
مسرحي إيثيل الليس للمدة
ملحق ١ يوم ٣ (ادمج مع الجسم).

4. Contraceptives (CPs): 2 Types

* A. Minipill → Contain Progesterone alone (Progestin)
* تغطية → B. Multipill → Contain Estrogen + Progesterone.

Estrogen:

- usually in the form of Ethinyl Estradiol (EE).
- All Estrogens acting as Androgen inhibitor by Many Mechanisms:
  1. ↓ GnRH Sec. → ↓ FSH & LH → ↓ ovarian T. products.
  2. ↑ SHBG → ↓ Free T.
  3. Direct ✲ Effect of T. on S.G.

Progesterone: has 3 Types (the 1st Type High should be avoided)

(1) ↑ Androgenic Progestins: has marked androgenic effects e.g.

- بيئيلز جينا Norgestrel & Levonorgestrel.
- MPA.

(2) low Androgenic Types

- [Gestodene.
- Norgestimate]
- [Desogestrel (much low)
- Northindrone.]

(3) Anti-androgenic Types:

- Drospirenone
- Cyproterone acetate.

OCPs لازم تكون الناس مسر
مسر لفع ليروجسترون
الأوفطار ع اسوم

- Yosmin
- Diane
- Drospirenone
- (FDA) → Cilest (Norgestimate)
- Marvelone (deso. gestrel)
- Gynera [Gestodene]

Progestrone: Androgen Inhibitor (-- FSH, LH) 5α reduct & antiandrogen (-- ARs)

Drospirenone 3mg + EE { 30 µg → Yasmin / 20 µg → YAZ } -- AR, -- 5α reduct.

Spironolactone, a synthetic steroid, is an antiandrogen that competitively binds to androgen receptors, inhibits 5á-reductase activity, and reduces androgen biosynthesis. This agent, in doses of 50-200mg/day, has been shown to be efficacious for acne, although the trials have been small, and differed in dosages evaluated, outcome parameters, and reporting methodology.1 Drospirenone (DRSP) is a novel progestogen derived from spironolactone and has both antiandrogenic and antimineralocorticoid activity. DRSP 3mg has been combined with two different doses of ethinyl estradiol: 0.030mg for Yasmin®, Bayer HealthCare; and 0.020mg for YAZ®, Bayer Schering Pharma AG. Yasmin® was recently approved for the treatment of acne in Canada, while both formulations are available in the US. For antimineralocorticoid activity, the dose equivalence for DRSP 3mg is spironolactone 25mg.[6]

Flutamide : (62.5 - 125) ، S.E قوي ضد تأثير الهرمونات

Flutamide is a non-steroidal androgen receptor antagonist indicated for the treatment of prostate cancer and has been found to be effective for treating hirsutism.[28-31]

Flutamide may be used for the treatment of mild to moderate acne. It should be used at low doses; 62.5 mg or 125 mg per day have been shown to be effective. The combination of OCPs and flutamide is likely more efficacious than flutamide alone.[32] In hirsute women with acne who were treated with OCPs, the addition of flutamide was significantly more effective than spironolactone.[33]

The potential for hepatotoxicity limits its use. However, no cases of fatal hepatotoxicity have been reported with doses less than 500 mg per day.[30] There have been reports of mild, transient liver impairment at doses ranging from 375-500 mg per day.[34,35] Women should remain on OCPs for birth control purposes as feminization of a male fetus can occur while on this medication. Patients should be off the medication for 3 months before conception.

"ممنوع حمل لمدة ٣ شهور بعد توقفه"

(قراءة) Contraceptives prescribed in AV (choice acc. to progesterone type).

FDA approved (٣ أنواع) (غير مجموعين بالسرق المصري)

- Estrostep (EE + Norethindrone)
- Orthi Tri Cyclen (EE + Norgestimate)
- Yaz (EE + drospirenone). (3 mg / 20 مكرو)

Non FDA but effective (بتاع yaz قبل)

- yasmine (EE + drospiren)
- Diane (EE + Cyp. A)

في مصر

- Cilest (EE + Norgest)
- Marvelon (EE + Desogest)

- **S.E of O.C.Ps:**
  1. **General (d.t EE):**
     - headache, nusea, wt gain.
     - Breast Enlargement & Tenderness.
     - Thromboemboli. Moode swings.
  2. **Drug interact & CPs failure:**
     - CYP 450 inducers may → failure (ex): Rifampacin, Griseofulvin, penicillins & Tetracycli
  3. **Other S.E:** dementia, MI, Stroke, Cancer breast.

5. Gonadotropin Releasing Hormone Analogs:
(Leuprolide & Nafaline)

Both → initially ↑ FSH & LH for 2-4 wks then sustained inhibition of FSH & LH → ↓ Androgen production by ovaries.

- dose: Leuprolide: 1 mg IM daily
  - Nafareline: 400 ug Intranasally / Twice daily.

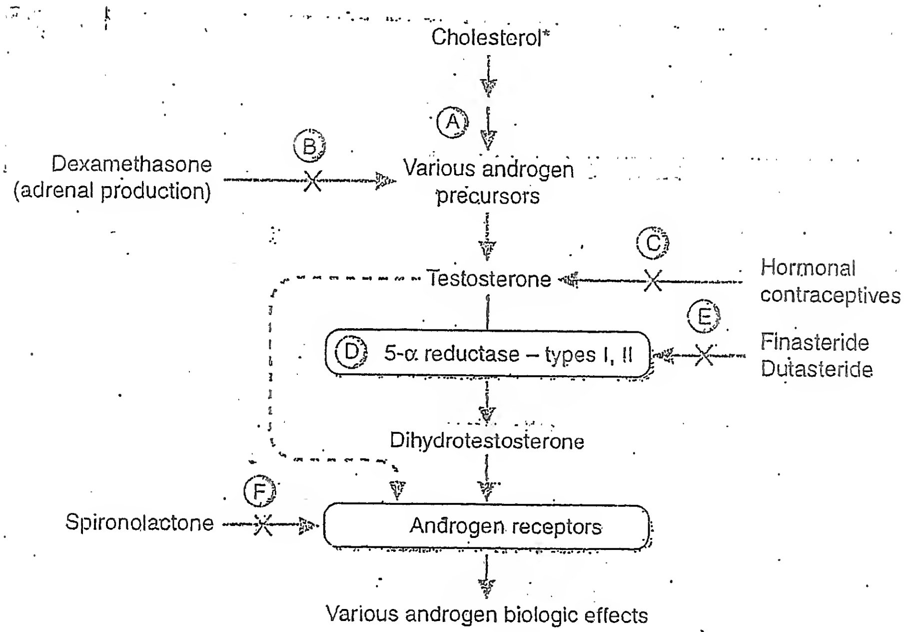
- disadv. Expensive & not well studied.

حلو

6. Herbal Remedies: (Antiandrogen & Androgen --).

- Saw palmetto
- + Green Tea. (تشرب شاي أخضر كثير كثير)
- Pygeum (AGA ← تستخدم علاج بروستات). (60-500 mg /d.)
- Stinging Nettle. (50-100 mg /d)

disadv.: Not proved by clinical Trials to be safe & effective.



* In mammalian cells, cholesterol is an essential cell membrane component (analogous to ergosterol in fungal cell membranes) and a precursor of all steroid hormones.
A Pertinent to androgenic steroids, cholesterol is converted to various androgen precursors such as DHEA and DHEA-S.
B Dexamethasone (and other corticosteroids) can inhibit the adrenal gland production of these androgen precursors.
C The ovaries can metabolize these precursors to testosterone; through negative feedback inhibition, hormonal contraceptives can ↓ ovarian testosterone production.
D 5-α reductase converts testosterone to its more biologically active form dihydrotestosterone.
E Both finasteride (type II 5-α reductase) and dutasteride (types I and II 5-α reductase) ↓ conversion of testosterone to dihydrotestosterone.
F Both testosterone and dihydrotestosterone bind to the androgen receptor; spironolactone competitively ↓ binding of both of these hormones to the androgen receptor.

Figure 23-2: Antiandrogen and androgen inhibitor mechanisms.

- Finasteride & Dutasteride → see AGA.

NB: duration of Hormonal Ħ → ≥ 3–12 ms.

Isotretinoin (systemic)

(13 Cis-retinoic acid)

Indications

1. Acne Vulgaris if:

- Severe < Nodulocystic / massive inflamm. → scarring
- Moderate: < Resistant or Relapsing = after 3 ms of conventional combined oral & topical antibiotic.
- Tendency for scarring.
- Psychologically distress of (Acne Excoriee)

(ينفعهم عشان نفسيتهم)

2. Acne variants: (severe types):

- Acne conglobata,
- " Fulminans → "لازم قبله ياخد Cs"
- Hidradenitis supp.
- G-ve folliculitis.
- Pyoderma faciale
- Severe Acne Rosacea.

Mechanism

(يشتغل على كل مكونات Acne)

(الأهم) ↓ sebum production (also normalize linoleic acid level)

- Normalization of follicular epith. desquamation. [Comedolytic] (أهم حاجة)
- ↓ P. acnes.
- Antiinflammatory

(Anti kerat. / inflamm. / < sebum, P. Acnes)

Dose: 0.5–1 mg/Kg/d for ≃ 5 month [4-6] (till cumulative 120mg/Kg)

- Acne conglobate: needs 2 mg/Kg/d
- Start ē 0.5 mg/Kg/d at start of Ħ (أول شهر) To avoid flare. (أول ٢-٣ أسابيع)

Regimens

Continuous Regimen

- Indications: as before
- Dose: Start c 0.5 mg/Kg/d for 1m (to avoid flare) & → ↑ gradually as the patient tolerate (max: 1mg/Kg/d) & Continue till a Cumulative dose 120–150 mg Kg/Course
- Course: 5 months (4–7 m.)

• يعني عبر طلاج : هوالـــــــــ :

Cumulative dose 120mg/Kg ω gives maximal Remission. (Now it's ↑↑ to 200 mg/Kg)

NB: Acne Conglobata: Needs 2 mg/Kg/d.

Intermittent Regimen

- Indications: ← ٣٠ فقرة
  1. mature adults c late onset Acne
  2. mild–mod. Acne
  3. inability to Tolerate S.E of Continuous regimen.
- Dose: 0.5–0.75 mg/Kg/d

يوميا لمدة اسبوع ثم راحة ٣ اسابيع وتكرر العملية (الفترة ٦ شهور)

(أو) نفس الجرعة يوميا لمدة ٤ ايام ثم راحة ٢٠ يوم [شريط كل شهر]

★ Effective

- 80% → resolved
- 40% → relapsed after 1Y.

(أو) • 0.3 – 0.75 mg/Kg/d For ≃ 6 ms

(Efficacy)

. The only Acne ℞ that's not open ended (leads to remission that lasts for ms – Ys.).

• Results of one study after Isot. Course:

- 40% → remains clear without ℞ for 3 Ys.
- 16% → Need Topical medication only.
- 25% → ~ oral Antibiotics
- 20% → ~ another Isot. Course.

• Relapse more common in:

- Age < 16
- Adult women
- pts. with mild Acne.

→ Best Treat. c Hormonal ℞

S.E (more details see Retinoids Therapy)

- Alopecia (T.E).
- Cheilitis → (90% ; most common S.E و لونا باحمرار)
- Dermatitis → مرطب باستمرار أو كورتيزون
- Pruritus
- Pyogenic granuloma (Pseudo PG).
- Eye : Xerosis (لازم تقلع العدسات وتستعمل Artificial Tear)
- Nose → Dryness → Crustation → Staph. aureus Colonization (90% of pts) (نستعمل فيوسيدين أو باستراسين حول فتحتي الأنف بريتن يوميا)
- Depression, Psychosis & suicide.
- Arthralgia & Myalgia.
- Impaired Night Vision.
- Pseudo Tm Cerebri (حالي)
- Pregnancy : Retinoid Embryopathy : abnormalities of : (50%)
  - Craniofacial (skeletal)
  - C.V.S
  - CNS
  - Thymus

آخر E

تأجيل أي عملية جراحية أو جلسة حتى شهر ↑ Tendency for Keloid.

Bone
- Premature Closure of Epiphysis (# أطفال)
- DISH : Diffuse Idiopathic Skeletal Hyperostosis (melted Candle wax on X-ray)

- Lab abnormalities : ↑ Liver enzs . ↑ Lipids < TG (++) / Cholest (+) ± leukopenia.
  (TGs ↑↑ more common)

Drug Interactions

ممنوع نهائيا تعطى معاهم ٣ أدوية
- Vit A → Toxicity (But Beta Carotene may be allowed).
- Tetracyclines → Pseudo Tm Cerebri
- MTX → additive liver toxicity

Pre ttt assessm. & Monitoring

- Pregnancy test : قبل العلاج ٢ اختبار ثم اختبار كل شهر
- CBC & renal : مرة كل شهر لمدة ٣ شهور ثم مرة كل ٣ شهور
- (2L) Lipid < Cholest / TG , Liver : مرة كل اسبوعين لمدة شهر ثم مرة كل شهر لمدة ٣ شهور ثم مرة كل ٣ شهور

C.I

- Pregnant
- Lactating
- Liver impairment
- Kidney "
- Alcoholics (risk of Hyperlipid)
- DM
- Hypersensitivity
- Hypervitaminosis A
- Hypothyroidism ??
- Children (ليه)

- ممنوع الحمل أثناء العلاج والفترة شهر بعد وقف العلاج !!

NB

① Fatty meal .لازم بعد] بيزود امتصاصها
. " " آخر وجبة في اليوم] للعفن

② لازم نبدأ بـ 0.5mg/kg لمدة شهر
To avoid flaring of Acne

. if Flare occurs → : ?? ... 0.25 ونبدأ بـ

. ↓ dose (0.25mg/kg/d) or stop

. Add CS, 0.5-1mg prednisolone

For 2-3 ws → Slow ↓ over 6 ws

Risk of Flare
. Macrocomedones
. Nodules.

③ Presence of mucocut. S.E → indicate good abs.

④ Isotret ± given:
. For children & neonates
. 5 courses ; ± needed

. Slow Response to Isot:
1. Macrocomedones → نعالج Electrocautry.
2. Nodular Acne
3. persistent deep pustules → نعالج Antistaph antibiotic.

. Isot. Related Flare:
. Exacerbat^n of AV.
. A. fulminans → نشيله سبقا بتقليل جرعة Isot. وإعطاء CS معاها.
"Paradoxical"

. NB: worsening of AV by ⟨ Isot. ?? / Antibiotic ?? (هامة جدا)

تحريد - ضمان

iPLEDGE™
Committed to Pregnancy Prevention

Have Questions? Call our toll-free number 1-866-
Monday to Saturday, 9 AM - 12 AM (Mi

1. للطبيب اللي يكتب.
2. للصيدلي اللي يصرف.
3. للمريض اللي بيتعالج.

SAFETY NOTICE

Isotretinoin must not be used by female patients who are or may become pregnant. There is an extrei high risk that severe birth defects will result if pregnancy occurs while taking isotretinoin in any amour even for a short period of time. Potentially any fetus exposed during pregnancy can be affected. Ther are no accurate means of determining whether an exposed fetus has been affected. Because of this toxicity, isotretinoin can only be marketed under a special restricted distribution program. This prograi called iPLEDGE™. Under this program, prescribers must be registered and activated with the iPLED(

Login for registered users

Username:

Password:

Forgot Password?

LOGIN

Register

Enter here to register in the iPLEDGE Progr for the first time or to change data on your registration form.

For Prescribers | For Responsible Site Ph

How to Report

Call our toll free number 1-866-495-0654 to report any of the following:

An Adverse Event: If you or someone you know has experienced an adverse event, please 866-495-0654.

A Pregnancy: If you are an activated prescriber, report pregnancy results by logging in and on "Manage Patients." Otherwise, please call 1-866-495-0654.

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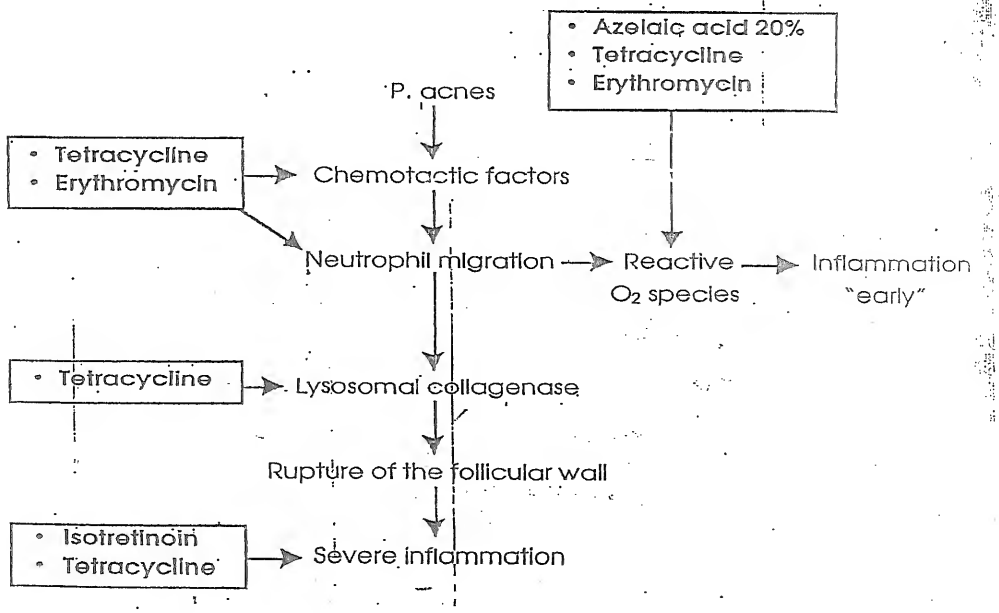
(4) Anti-inflammatory effects of acne therapy

المحور الرابع للعلاج



2. Physical measures

- UVR
- Extraction of comedones: comedo extractor, light cautery after EMLA (local anaesthesia) application.
- Superficial freezing with liquid nitrogen.
- Intralesional corticosteroid injections (in lesions < 7 days old). ⟷ 2.5 mg/ml
- Cryotherapy. (lesions > 7 ds old)
- Cosmetic camouflage.
- post acne scars.

3 Lasers, Lights & Acne.

Mechanism either:

destroying P. Acnes through photodynamic reaction (PDT)

- Photoexcitation of Coproporphyrin III (produced by P. Acnes) ⟶ generate of Singlet oxygen (Free radicals) ⟶ destruction of P. Acnes.

- Types:
  1. Blue light Sources (405-420 nm)
  2. Red light " : (660 nm).
  3. Combined Blue & red.
  4. Green light lasers. (582 & 532/1064)
  5. yellow " " (low fluence pulsed dye 585-595 nm)
  6. IPL
  7. Radiofrequency (RF) devices.
  8. PDT (Blue light & ALA).

- Blue light (intense violet) [405-420] ⟶ the best & approved by FDA.
- NLite III: (585)

destroy the Sebaceous glands

↳ PDL (by broad band light 550-700 nm)

- Types:
  1. near infrared lasers
  2. 1450 smooth beam lasers.
  3. IndoCyanin green (ICG) + diode laser (810-900 nm)
  4. 1540 Erbium glass
  5. RF devices.

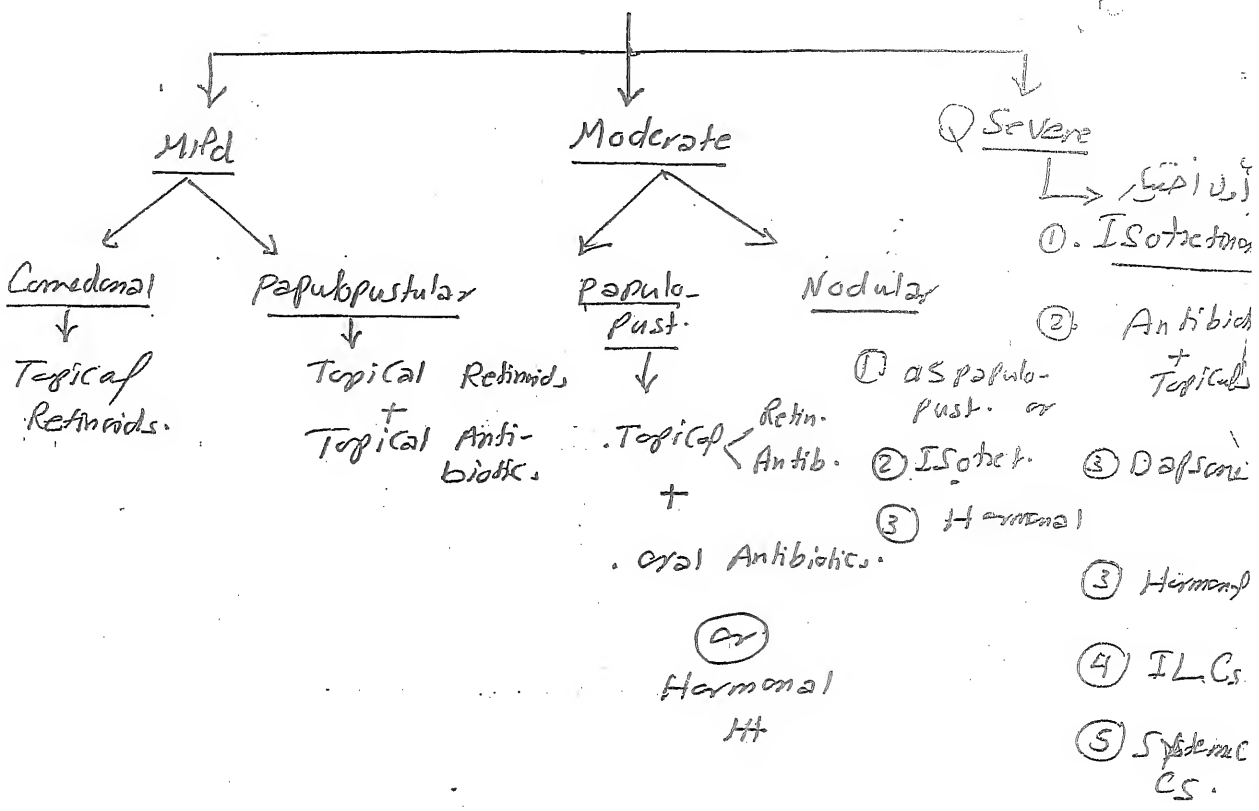
Severe Acne:

- Nodulocystic Acne (Acc. to WHO Severity C

بعد استعراض خطوط وأنواع العلاج

↓

هنختار العلاج على حسب درجة "Acne"



. Treatment of Severe Acne ?? (امتحان)

NB Nodulocystic lesions

- < 7 d. → ILCs (2.5 mg/ml : 0.25 = 0.1 ml)
- > 7 d. → Cryo (2 Cycles; 15-30 sec.)

NB "Sig Exp"

- **Acne & pregnancy:**
  - Pregnancy < Early: Exacerbate Acne
    late: ↓ Acne (↓ ↑ Estrogen).
  - **Safe drugs:** Erythromycin, BP, Azelaic acid.

- **Indications of Cs in Acne:**
  1. **Topical Cs:** for Severe inflammed papules.
  2. **IL Corticosterid:** for Nodulocystic acne.
  3. **Systemic Cs:** for Acne fulminans.
  4. **low dose " " :** ↓ Suprarenal Androgens. (Dexameth.)
  5. ē Isot. to ↓ Flare

- **Non Isotretinoin tt of Nodulocystic Acne:**
  1. **Dapsone** (50-100 mg/d)
  2. **IL Cs**

(Ask)

- **Indications for Hormonal assessm. of Acne Cases:**
  1. Irregular menest.
  2. Other androgenic Manifs. Hirsutism & AGA
  3. Rapid relapse after Isotretinoin.

5) Pyoderma faciale (Rosacea Fulminans).

HH

1. ISotret.
2. CS (Topical & Syst.)
3. Dapsone
4. Hormonal HH (♀).

Mx of Rosacea

A. Instruct (X Avoid)

- Hot, Humid
- emotional stress
- Hot drinks
- Alcohol
- Spicy food
- # Sun protect Pgs

B. Manage Inf. the Rosacea (Acc. to the type)

(i). Flushing: - BB, Clonidine, SSRIs

(ii). Telangect: Laser, IPL

Brimonidine eye drops

(iii). Papulopust. Lesion

- low dose tetracycl (4 wks) /Doxy 0-75(-1)
- Topical Metronidazol (Rosa 2)

))

Azelaic acid

(iv). ocular Rosacea:

Other lines

(1). Ivermectin lot- (FDA)
(2). Ectomethrin.
(3). Crotamiton.
(4). Sulphur soln 1% in Calamine CLT
(5). Isot-
(6). Topical Anti
(7). Retino-
(8). Fungal - soln

Rhinophyma

- Surgery.
- CO_2.
- Dermabrasion
- Isotret-

FDA — Ivermectin lot
Brimonidine

NB④ Bacterial Resistance in Acne.

- Common problem with AV.
- **Classificat. Acc. to degree of Resistance:-**

① Common
- [Erythromycin.
- [Clindamycin.
- Tetracycline
- Duxycycline. — لو الوام بس يحل لكلاتين

② less Common
- Minocycline
- Zinc + Topical.

③ No Resistance
- BP
- Azelaic acid
- Isotretinoid

- **How to limit bact. Resistance in AV??**
  - limiting durat. of tt.
  - Good Compliance.
  - don't leave the antibiotic except if lost its efficacy.
  - (كاملة) avoid use of dissimilar Topical & systemic antibiotics.
  - use Isotretinoin.

- **NB2: what is Severe Acne,**

① تعريفه حسب جدول (Severe A. Vulgaris).
Acne severity classif.

② A. Conglobata

③ A. Fulminans

④. G-ve folliculitis

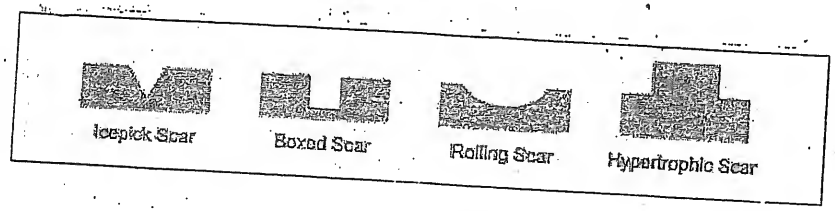
⑤ Pyoderma faciale (Rosacea fulminans)

Complications of AV & its Management.

Psychological

1. depression
2. Dysmorphobic Acne. (disturbed Image)
3. disturbed social relationship.

Post Acne scars. (4 types)



	Definition	Treatment
Ice pick scars (most common type)	pitted scars: It is due to the loss of part of the epidermis so that the skin 'dimples' slightly.	* Dermabrasion * Laser resurfacing * Punch grafting for deep scars. * Subcision®: a surgical (technique in which the fibrous band under the scar is divided, allowing the skin to return to its normal position). * Larger scars can be excised (cut out)
Atrophic scars (craters).	flat, thin scars. occurs when the epidermis is 'captured' by the scar tissue of a deeper acne lesion and is pulled into a deeper pit.	* Soft tissue augmentation techniques *such as* hyaluronic acid, collagen, gelatin matrix & fat implants * Dermabrasion
Hypertrophic(keloid) scars	thick lumpy scars	* Potent topical steroids for a few weeks * Intralesional steroid. * Silicone gel dressings * Cryotherapy * Surgical revision

Dermatological

(AP | IS)

- Solid facial Edema → Isotret + Ketotgen.
- Persistent Erythema → IPL
- Postinflammatory
  - Hyper Pigm. → Bleaching Creams
  - Hypo-Pigm. → leave For Time.

(NB Solid facial Edema: (Morbihan's dis.):

- An unsual & disfiguring complication of AV.
- C/P → · swelling & Erythematous non scaly woody induration of soft tissue of midline of the face & cheeks
  - No Spontaneous resolution.
- Causes: 1- AV
  2. Rosacea
  3. Melkersson Rosenthal synd.
- Rx → Isotret. (0.2-0.5 mg/kg) + Ketotifen (1-2 mg/d) for 4-5 m.

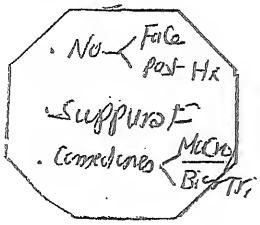
Etiology: damage to Lymphatics of face 2ry to AV

[Similar to cellulitis of Legs]

[Complete Article on DOJ] (2008)

Acne Variants

1. Acne Conglobata:



- dpf. Severe Eruptive Nodulocystic Acne without Systemic manifestations.
- Usually affects males (20-25 yrs) with No Past Hx. of Acne.
- CIP: Severe Nodules, Cysts & Comedones (Macro → (grouped bihead or Trihead) on Trunk (back, FaCe) → large abscesses, Sinuses, Kelloids & Sca.
- Rx: 1. Isotretinoin 2 mg/kg/d for 5 mo.
  2. Corticosteroids (oral & IL).
  3. Dapsone.

NB: Acne Conglobata may be part of:

1. Follicular occlusion Triad or tetrad.
2. PAPA Synd.
3. SAPHO Synd

Part of a related group of inflammatory disorders that include:
- Uveitis
- IBD
- PS

- Arthritis مع AV مع التهاب:
  - A. Fulminans
  - PAPA Synd.
  - SAPHO "

4. PASH Synd: PG, Acne, Suppurative Hidradenitis.

1. Follicular occlusion Triad:
   - Acne Conglobata
   - dissecting cellulitis of scalp → Triad
   - Hidradenitis suppurativa
   - Pilonidal sinus → Tetrad.

2. PAPA Synd: Pyogenic arthritis + Pyoderma gangrenosum + A. Conglobata (or fulmin.

Rx
- Immunosuppressives
- Retinoids
- Infliximab

3. SAPHO Synd:
   - Synovitis
   - Acne (Conq. or Fulminans).
   - Pustulosis
   - Hyperostosis
   - Osteitis.

4. AHYS: Acq. Hyperostosis Synd

PAPA

Threonine

Interacting protein

Genetic mutation in PSTPIP

proline Serine phosphatase

or CD2BP1 gene. (Actin organization & maintain proper inflamm. response)

Acne Fulminans (Acne Maligna) = Leukemoid Reaction

No face / Past Hx / Hgic ulcers = Systemic manifs.

- Most severe form of Cystic Acne that is ass. with systemic manifs.
- clinically: (sudden onset):

• Severe Systemic manifs

- FAHM
  - Arthralgia
- Anemia
  - leukocytosis
  - ↑ ESR
- HSM
  - Bone: → Osteolytic lesions.
- Proteinuria & Haematuria

• Severe Cut manifs. (Acne)

- Early: Acne Conglobata like lesions
- Later on: Hgic Nodules & Plaques → suppuration & ragged ulceration (Hgic ulcers).
- (Face less affected)

Treatment.

1. Hospitalization.
2. Wound
   - debridment.
   - Warm Compresses of 20-40% Urea
   - Topical Antibiotics
   - Topical superpotent Cs.

Systemic Cs (short Cus) steroid
till control → Add Isotretinoin
2ws → discontinue the Cs
Isot. (like methotrexate)

0.5-1 mg/kg/d
Max Cumulative dose: 120 mg/kg

Pathog.: Acute Febrile systemic complicat° of Acne conglobata induced Immunologically by P. Acnes Ag & predisposed to by: Androgens, IMN, Isot.

	Acne conglobata	Acne fulminans
• Sex	• Men > women	• Men
• Age	• 20-25 years, Nos past Hx	• 13-16 years ± Past Hx
• Onset	• Slow	• Sudden
• Localization	Fac & Trunk	- Trunk
• Clinical features	• Nodules, cysts, polyporous comedones	• Hemorrhagic ulcerations
• Systemic signs & sym.	• Uncommon	• Very common, malaise, fever, leukocytosis, elevated ESR, polyarthralgia, osteolytic bone changes, proteinuria, erythema nodosum, hepatomegaly, splenomegaly
• Response to systemic antibiotic therapy	• Yes	• No

NB. ± ass e EN.

DD. Acne Fulminans like flare Induced by Isot.

3 Gram-ve folliculitis: (2015)

- Superficial pustular or Nodulocystic eruption grouped around the ant. N ares occurs as a Complication of prolonged ttt of Acne with broad spectrum antibiotics (which colonize these bact.).
  - (i). follicular pustules
  - (ii). Nodular lesions
  - (iii). Worsening of Acne
- AET → G-ve bact. / E-Coli / Pseudomonas / Proteus / Klebsiella. (Enterobacter)
- Treatment: 1. Stop the current antibiotics
  2. TMP: 400-600 mg id or Amoxicillin
  3. Isotretinoin: for resistant cases.

- Etiopathogenesis:
  1. Antibiotics + Moisture (created by Sebaceous media) → ↓ G+ve flora (staph & diphtheroids) → ↑ G-ve bact. (from 1% - 4%) at ant. N ares.
  2. Hypersensitivity reaction to microbial Ag. (↓ IgM & ↑ IgE)

- If Suggestive History either:
  1. Nodulocystic AV. (e) non response to Antibiotic
  2. Responsive AV → sudden flare following either cessation or reinitiation

- If lesions either:
  1. Superficial pustules (e) cut Comedones (80%) = Other G-ve bact.
  2. Deep Nodulocystic lesions → "Proteus"
  3. Generalized G-ve (e) Hx of Hot tubs or Swimming pools → (P)seudomonas

IVs:
- G-ve Stain & Culture (e selective media of MB like methylene)
- Biopsy

ttt → Best by Isotret.?? has No Antibact effect but ↓ Sebum → ↓ Seborrhea → ↓ moisture → unfavorable environment for G-ve.

	4. Neonatal Acne	5. Infantile Acne
Incid.	• 20% of healthy Neonates	• ♂ > ♀ ; ± FH of severe AV.
onset / resolution	• Start 1st 2 ws & resolve within 3 ms. (2 ws – 3 ms)	• Start : 3 – 6 ms & resolve within 1 – 2 ys (but) may persist to Adolescence.
C/P	• Inflammatory papules on cheeks & nasal bridge • No scarring nor ↑ incid. of Acne later on.	[usually Comedones. [occasionally : Nodulocystic • ± scarring & ↑ incid. of Acne in later life
Pathogenesis	• Controversy : ± d.t 1. Malassezia (Furfur & Sympodialis) والدليل بتحسن اللى بيحصل مع كيتوكونازول. So some named it ; « Neonatal Cephalic Pustulosis ». 2. ↑↑ Sebum secretion during this period.	may be d.t : 1. ↑ LH & T. during 1st 6 – 12 ms ([illegible]) 2. Immaturity of supra-renal glands → dis proportionately large Zona reticularis → ↑↑ DHEA-S (The level of [illegible] ↓↓ at 1 year till Adrenarche)
Tt	① reassurance (self limiting) ② Ketoconazole 2% Cr. ③ Benzoyl peroxide	① Retinoids. ② Benzoyl Peroxide ② Isot. (if Nodulocystic).

"Acne According to Age"

Age group	Location	Morphologic condition	Sex
Neonates	Nose, cheeks, forehead	Comedonal + papules	Both
Infants	Face	Inflammatory	Males
(Childhood) Preteens	Centrofacial	Comedonal	Both
Teens	Face, trunk	Mixed	Both
Adults	Perioral, jawline, chin	Inflammatory	Women

Adults → "Postadolescent Acne" > 25 ys.

Variants of AV
(Acneiform Eruptions)

Type	C/P
1. A. Conglobata 2. A Fulminans 3. G-ve folliculitis 4. Neonatal Acne 5. Infantile Acne	→ see before
6. Childhood Acne (Juvenile) (2 - 7 ys)	• Etiology 1- Precocious puberty → Hormonal & Assay 2. Acne Cosmetica بيطلع ع أماكن اللي بيتحط عليها حاجة • C/P: Comedonal
7. Acne Mechanica	• occurs 2ry to repeated Mechanical Trauma To the pilosebaceous outlet → obst. → Comedo formation. • ممكن نشوفه في شكل خط نتيجة الاحتكاك مع: • bra straps • helmets الخوذة • violins neck • الطرحة والإشارب • [illegible] Tt → Avoid Trauma
8. Acne Excoriee des Junes Filles (Picker's Acne)	• usually affects women c̄ Anxiety, depression or obsessive compulsive disorders. • C/P: 2 Types < No lesions or mild n (Comedones + Papules) → psychosis anxiety squeezing, picking scratching → linear & Geometric Erosions, Crustation & scarring Tt < ① psychotherapy ② Antidepressants [SSRIs, Prozac, Motival] ③ Acne Tt → Isotretinoin [aggressive Tt Needed]

X-Ray on Bone ??

Type	
9. Occupational Acne	Occupational Exposures to Comedogenic Substances e.g Cutting oils, (Coal tar) Petrolatum products [tar Acne] (ع زيوت إسكانية)
10. Chloracne	• Occupational exposure to Chlorinated Aromatic Hydrocarbons in: [• Electrical conductors & insulators • insecticides, fungicides & herbicides • Wood preservatives.] (دهانات) • CIP: Small cystic papules & Nodules at retroauricular, Manbibular, axillae scrotum. • Healing ± → Scarring. • Hx ① Stop the Exposure. ② Antibiotics, Retinoids & Isot. Hx.
NB: Contact Acne: • Mechanica • pomade • Cosmetica • occupational (tar)	
11. Pomade Acne (زيوت عطرية)	نتيجة استعمال بزيوت وبكريمات دهنية على الشعر فتنزل على الجبهة (وجه جيد)
12. Acne Cosmetica (A. Venenata)	تأثيرات التجميل التي تكتوي بـ: Lanoline, Petrolatum, oleic acid → (Comedogenic Agents)
13. Acne Detergents	→ d.t detergents e.g Hexachlorophene in Soaps → Papulopustular Eruptions.
14. Acne Aestivalis (A. Mallorca) (Summer grape in North america)	• affect women in North america • Start in spring → progress in Summer & resolve in winter. • inflammatory Papules (no < Pustules / Comedones) on cheeks & Neck.

15. Acne Medicamentosa

[Drug induced Acneiform Erupt]

سؤال امتحان

Differentiate bet AV & Acneiform Erupt:

- Abrupt onset
- Hx of drug intake.
- Not at classical sites of Acne (Face) but at Neck, Trunk & arms).
- Monomorphous follicular papulopustular ē Comedones (..) — AV is (polymorphic)
  [Inflammed papules & pustules ē Sparse-Absent comedones].
- More common postinflammatory Hyperpig.
- resolve ē stop of drug.

Ht:
- Stop the drug
- Tretinoin 0.05% (1-3 ms)
- Antibiotics.

(sudden flare)

Drugs reported to cause acne or acne-like eruptions (Acne medicamentosa)

Hormones and steroids	***Antituberculous drugs***
• Gonadotrophins	• Isoniazid
• Androgens	• Rifampicin, Tetracycline
• Anabolic steroids	***Miscellaneous***
• Oral and topical steroids	• Chloral hydrate
Halogens	• Cyanocobalamin
• Bromides	• Disulfiram
• Iodides	• Lithium
• Halothane	• Psoralens (with UVA)
Anti-epileptic drugs	• Quinine
• Diphenylhydantoin (phenytoin)	• Sulphur
• Phenobarbitone	• Thiouracil
• Troxidone	• Thiourea

EGFRs inhibitors

Vit B1, B6, B12, D2.

NB ① Cs: . Topical or systemic → Erupt.
. Systemic Mod-long Dexameth. For ≥ 3-5 ds → Erupt

Cs induced Acneiform ← Acne Rosacea / Acneiform Erupt

② Bromides: Sedatives, Analgesics

③ Iodides: ~ ~ : Cold drugs, Vitamins, contrast dyes.

3. Radiation Acne: "كيلت"

- Comedo-like papules d.t Exposure to ionizing Radiat=.
- starts to appear as the acute phase of radiat= dermatitis begins to resolve.
- Mechanism: Radiat= → epithelial Metaplasia in the follicle → Hyperkeratotic plug.

HL 4. Apert Syndrome [Acroencephalo syndactyly]:

- Androgen → ↑ AV, ↓ Early epiphyseal Closure.
- AD disorder ch: By disfiguring Synostoses of ! bones of hands, Feet, Vertebrae & Cranium. (↓ Abn. joint development)
- This disorder may be ass. w/ th... Cut. manifs. as:
  - Seborrhea.
  - Nail dystrophy.
  - Hypopigmentation.
  - Acneiform Erupt=: (Extensive).
  - Nevus Comedonicus. ✓

d.t Mutat= in FGFR2 gene.

- Facies: Flattened occiput, Parrot-Beaked Nose.
- fused, shortened digits.

5. Transverse Nasal Crease: (pseudoAcne).

The transverse nasal crease is a horizontal anatomical demarcation line found in the lower third of the nose which corresponds to the separation point between the alar cartilage and the triangular cartilage. Milia, cysts and comedones can line up along this fold[33]. These acne-like lesions are not hormonally responsive and arise during early childhood prior to the onset of puberty. Treatment consists of surgical expression as needed.

X 6. Idiopathic facial aseptic granuloma :

A chronic, painless, solitary nodule, reminiscent of an acne nodule, appears on the cheeks of young children. The mean age at presentation is 3.8 years. Multiple lesions are uncommon. Histopathology reveals a chronic dermal lymphohistiocytic infiltrate with foreign body-type giant cells. Cultures are typically negative (70% of patients) and the lesions do not respond to antibiotic therapy. The nodules resolve spontaneously, after an average of 11 months, without treatment[33a].

سؤال امتحان

Syndromic Acne (Acne Syndromes)

- Follicular occlusion Triad / Tetrad
- PAPA
- PASH
- SAPHO
- Apert Synd.
- SAHA ✓
- PCO
- Apert.

(14)

. Other entities (By Bolognia):

1. Epidermal Growth Factor Receptor inhibitor:

. def. group of Therapeutic Agents used for ttt of Solid Tms (Glioblastoma, head & neck cancer and lung Carcinoma) e.g 3 ← Gefitinib. Cetuximab. erlotinib.

• These Agents are ass. with Acneiform Eruption in most cases (≈ 75%) & it may indicate successful response to ttt.

• Clp: Eruptive Monomorphous follicular papules & Pustules involving face, scalp & upper trunk [No Comedones]

• Pathology: Folliculitis with intrafollicular Neutrophilic infilt. & perifollicular lymphocytic infilt.

CS in MD

• DD (Eruption in oncology patients):

1. Cs induced Acne.
2. Neutrophilic Eccrine Hidradenitis
3. Folliculodystrophy of Immunosuppression.
4. other forms of folliculitis (Pityrosporum & demodex).

• ttt: Antibiotics, Cs (Topical) & retinoids.

2. Tropical Acne: حب المجارين

. Acneiform Eruption d.t Exposure to heat (in tropical climate) or 2ry to scorching حرق occupational Environment (as in furance فرن workers).

• Clp: Follicular Nodulocystic lesions ∴ may be infected by staph. at Trunk & buttocks

• ttt: → Moderate of Climate.

Causes of comedones

1. **1ry developmental defect of the follicle:** Nevus comedonicus and Nevoid follicular epidermolytic hyperkeratosis.
2. **A genetically determined abnormality of pilosebaceous function:** Acne vulgaris and familial comedones (autosomal dominant with mono- and poly-porous comedones and seb. cysts).
3. **Disturbed follicular keratinization** produced by exogenous acneigenic agents: Acne Venenata and Acne medicamentosa.
4. **Injury to pilo sebaceous follicles by ionizing radiation,** e.g. cobalt.
5. **Connective tissue abnormalities:** pseudoxanthoma elasticum, solar elastosis "Favre-Racouchout", lichen sclerosis et atrophicus, Necrobiosis lipoidica.

The spectrum of acne & acne-related dermatoses

Acne related to intrinsic causes
- Acne vulgaris
- Perioral dermatitis
- Acne conglobata
- Hidradenitis suppurativa
- Acne fulminans
- Pyoderma faciale

Acne related to extrinsic causes
- Acne excoriée des jeunes filles
- Acne mechanica
- Acne tropicals
- Acne aestivalis
- Favré-Racouchot syndrome
- Drug-induced acne
- Acne cosmetica
- Pomade acne
- Occupational acne
- Chloracne

Childhood acne
- Neonatal acne
- Infantile acne

Acneiform eruptions
- Rosacea
- Acne keloidalis nuchae
- Gram-negative folliculitis
- Steroid acne

Rosacea

(سؤال امتحان مهم)

- **def.** Common Condition ch. BY Symptoms of facial Flushing & a spectrum of clinical Signs including Erythema, Telangiectasia, Coarsness of Skin & papulo-pustular Eruption resembling Acne.

- **Etiology & Pathophysiology:** → unknown but ↑ d.f: (عشان ايه)

  1. **Vasculature:** ↑ NO, ↑ Flow, VD.
     - ↑ NO & Flow of Blood in facial BV → Flushing.
     - Exaggerated VD response to Hyperthermia.

  2. **Climatic Factors:** (sun).
     - Harsh climatic exposure (as Solar irradiation) → damage to Cut. BV & dermal C.T.
     - this explain why it:
       - Worsens in Spring & Summer.
       - affect Facial Convexities.

  3. **Dermal Matrix degeneration & endoth. damage:**
     - endothelial damage & dermal Matrix degeneration → Poor Tissue support of Cut. Vs →:
       - pooling of serum → inflammatory mediators & Metabolic wastes.

  (dermal M. degen. ← leakage ← damage ايهما حدث اول هل [مش معروف]
  dermal Matrix degen. → lack of Vs support → endoth. damage. : ابدأ)

  4. **Microbial organisms:**
     - ⓐ **Demodex**: is a mite that NLLY inhabit the lumen of large Sebaceous follicles in areas affected by rosacea (Nose & Cheeks); an immune response Mediated by T-helper surrounding Demodex is Suggested (Controversy).
     - ⓑ H. Pylori (Controversy).
     - ⓒ P. acnes.

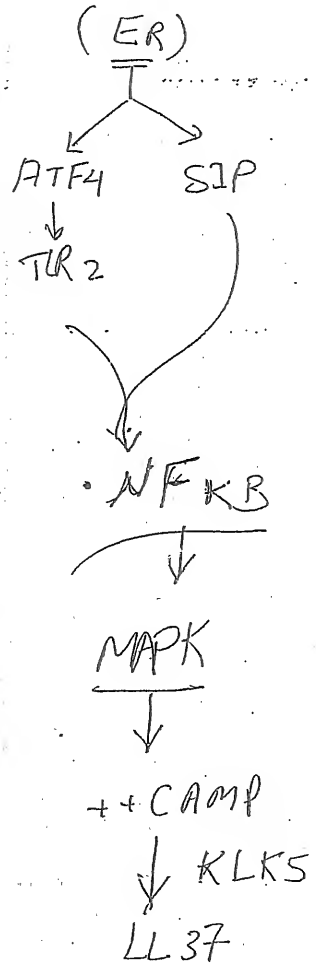
it role is exacerbating Factor in predisposed individuals.

Ecfonethrin improves Erythema & Papules not Pustules.

1. Vasculature
2. degen.
3. Climatic
4. Chemical & ingested agents.

2. Microbes.
3. Antimicrobial peptides.

↑ ROS
↑ ferritin.



- Metronidazole : -- Neut., ↓ ROS, -- KLK5
- Ivermectin : -- Demodex & MPAK
- Retinoids:

5. Anti Microbial Peptides: (AMPs): (2009) ↑↑

- def. Small MW proteins that are a part of innate Immune response & have broad spectrum antimicrobial Activity against bact, viruses & Fungi. they are released upon injury & for inf.
- These AMPs are as:
  - (A) Cantheli Cidins & β defensins → ↑↑ in Rosacea.
  - (B) LL 37 (peptide form of Cantheli Cidin) is Expressed by PMNL & Lymphocytes → ↑↑ in Rosacea → interact ē Endothelial cell → ++ Angiogenesis.
    - Modulate VEGF Expression.
    - its injection in mice → inflamm. Erythema & Telangiectasia.

Ayr (2009) 5

6. ROS:

- Neutrophils → ROS (superoxide anions, hydroxyl radicals, Singlet O., Molecular O, H_2O_2) → Tissue damage & inflammat°.

6

7. Serum Ferritin:

- Fe → ++ Conversion of H_2O_2 to free radicals, ēv → Tissue damage & inflamm.
- Evidence of ferritin role:
  - Biopsy from rosacea → ↑ No. of ferritin positive cells.

& higher ferritin positivity is ass. ē more advanced Types of Rosacea.

8. Chemical & ingested agents:

Spicy food, alcohol, hot beverages may Trigger Flushing (but these agents have No central role).

Perivascular & perifollicular inflamm. (Common).

- Epidemiology:
  - Age: → any (old & children) but Commonest 30-40 Y
  - Sex: → ♀ > ♂
  - Race: More in Fair skin individuals.

C/P of Rosacea:

- **C/P Includes:**
  1- **Features of Rosacea.**
  2- **Subtypes and variants of Rosacea.**

1- PRIMARY AND SECONDARY FEATURES OF ROSACEA
A- Primary features
• Flushing (transient erythema)
• Non-transient erythema
• Papules and pustules
• Telangiectasia
B- Secondary features
2. Burning or stinging, especially malar skin.
3. Plaques
1. Dry appearance, especially central facial skin
5. Soft or solid facial edema
6. Ocular manifestations 40%
7. Peripheral location
4. Phymatous change

Burning / Stinging / Xerosis
Plaques
Edema.
Rhinoph.

JAAD 2002

(1). Comparison bet Rosacea & AV

(2). Steroid Rosacea.

(3). LMOF

(4) Syndromic Acne.

- SAPHO
- PAPA
- PASH
- SAHA
- PCOS
- Follicular occlusion Triad or Tetrad.
- Apert.

2-SUBTYPES AND VARIANTS OF ROSACEA AND THEIR CHARACTERISTICS (National Rosacea Society 2002).

A- Disease subtypes:	Characteristics
1-Erythematotelangiectatic (Vascular)	Flushing and persistent central facial erythema with or without telangiectasia (Triggered by)
2-Papulopustular (inflammatory)	Persistent central facial erythema with transient papules and/or pustules (lasting 1-4 ds)
3-Phymatous	Thickening skin, irregular surface nodularities and enlargement. May occur on the nose, chin, forehead, cheeks or ears (start as dilated pores Vs + wide pores → Progress)
4-Ocular	Foreign body sensation in the eye, burning or stinging, dryness, itching, ocular photosensitivity, blurred vision, telangiectasia of the sclera or other parts of the eye, or periorbital edema, recurrent styes & chalazion.
B- Variants: 1-Granulomatous rosacea 2-Periorificial dermatitis 3-Pyoderma faciale 4-Steroid rosacea	JAAD 2002

NB on CIP

(A) Erythemo Telangiectatic Type: (وردية وعائية)

- Erythema: . is the earliest sign.
  - . affect central face & spare perioccular skin.
  - . acc. by stinging sensation
  - . start as intermittent → become long lasting then → persistent.
  - . skin is thin & lack sebaceous quality (that chic of Acne)
- Telangiect.: start at alae nasi → Nose → cheeks & may become large angiomas.
- NB: . Edema & induration is common.
  - . When Edema becomes persistent → woody induration occurs this is variant of Rosacea called: "Solid facial Edema, Rosacea Lymphedema (DD. that of AV).

Triggers
- Sun
- Emotional Stress
- Hot drinks
- Alcohol
- Spicy food.
- Exercise
- Hot or Cold weather . Topical

(i). Erythema:
Early → Transient (Flushing)
Later → Fixed

(ii). Edema:
Early → Transient
Later → Fixed (Morbihans)

(B) Papulopustular Type: (حبوب وجدرية)

- the classical Type.
- papulopustules similar to that of AV but differs in:
  - . dome shaped.
  - . deeper red color.
  - . No Comedones.

Ⓓ phymatous Rosacea:

- d.t Seb. gland hyper plasia.
- Types:
  - clinically : Nasal & Extra Nasal.
  - Histologically :(4)
    - glandular.
    - Fibrous.
    - Fibroangiomatous.
    - Actinic.

Ⓔ ocular Type:

ممكن تشتغل في الجلد بنسبة ولكن الأثر الأولاني مرشحان معاً.

- 50% of cut. rosacea show ocular S & S.
- Etiology: ① Meibomian gland impact → ↓ lipid content of tears → ↑ Evaporation → Eye irritability.
  - ② ↑↑ Matrix Metaloproteinase 9 in Tears (Doxy ↓↓ it → improvement).
  - ③ Tear film Acidity (ذكرها)

Q Variants of Rosacea

1. Granulomatous Rosacea:

- Large granulomatous Nodules or Very persistent, discrete red to brown Facial papules That show granulomatous inflamm.
- May be overlaped ē. LMDF. (lupus miliaris disseminatus Faciei) & Sarcoidosis
  الاسم الأفضل

"MIS-Diagnosed As perioral ECzema" ← 2. Perioral & (periocular (Periorificial) Dermatitis: (Oriel 2010)

- def. chr. papulopustular & ECzematous Facial dermatitis usually affecting Women but ± also affect Children
- Etiology: unknown but ± d.t.:
  1. Topical Cs.
  2. Cosmetics: مرطبات الجلد - كريمات الأساس - معجون الأسنان
  3. Physical agents: UV Rs, Heat, Wind.
  4. Microbials: Fusiform bact, Candida, H. Pylori, Demodex ← Controversy
  5. Hormonal: Menestruation & OCPs
  6. GIT disturbance (Malabs).

- Steriod:
  1. Acniform
  2. Rosacea
  3. Perioral Dermatitis

] Overlap

- monomorphous papules
- ± any pustules, scales, ECZematous patches

· Epidemiology: usually affects women 20-40 ys.
· Children may be affected. (Childhood granulom. Periorificial D)

· C/P: · grouped "follicular reddish" papules, papulovesicles, pustules on Erythematous base that ± show confluence.
· Site: · perioral (specially nasolabial) & periocular (lat. lower Eye lid) some times ē free border bet. the lesion & the vermilion boder of lips.
· Extra facial involvement may occur.

(· link to Rosacea is uncertain but: · Age & Histopath. ± similar · ± ass ē Rosacea.)

· NB: Ttt ① Stop the offending Agent:
② Tetracyclines, Topical Antib., Icst.

③ Pyoderma Faciale (Rosacea Fulminans):

(Linked to Rosacea d.t: · Same path. · " ttt.)

- sudden onset of
· Indurated plaques composed of grouped inflammed papulopustules at face.
· its similar to rosacea in:
· pathology & · ttt
· but differs from it in:
① Younger Age.
② More often ♀
③ No flushing.
④ No ocular sympts.
⑤ ttt → Cs (40-60 mg/d) · or Isotretinoin, ant. antibiotic

(M/s diagnosed as: · Pyoderma · leishmania · blastomycosis.)

4 Steriod Rosacea:

· occurance of Rosacea like lesions [or] Exacerbation of preexisting Rosacea in response to use of Topical Cs.
· if Cs used in rosacea:
· at first: → improves.
· lateron: → atrophy, persistent VD & inflammatory papules.

(NB) · Rosacea like lesions at upper lips + ala nasi → clue of Cs use.

H

① Stop Cs : [فجأة أو بالتدريج]
② Topical Parmoxine " non sensitizing local anaesthetic "
③. Soothing agents.
④. Topical Calcineurin inhibitors — على الرغم من إنها ممكن تعمل "Rosacea & ↑ Demodex Prolif."

. Add weaker Cs then stop. ← Flare up — وقف الكورتيزون فجأة ده ممكن يعمل
. Add Doxy.

• Histopathology of Rosacea:

① Mild: → vascular Ectasia & mild Edema of papillary dermis
② Advanced (Non pustular): perivascular & perifollicular lymphohistiocytic infilt.
③. pustular: Granulomatous inflamm. & ± Perifollicular abscess (non Caseating Epitheloid).
④. also ✓. ↑ Demodex.
✓. Seb. Hyperplasia.

• DD. of Rosacea:

① AV.
② SD.
③. L.E.
④. LMDF
⑤. Haber Synd.
⑥. Demodex Folliculitis.

1. AV: younger age, ♂ = ♀, Comedones, & Cyst, not exactly in central face, & Trunk, glossy skin
2. SD: greasy scales at Seborrheic sites. Sq. blepharitis may simulate ocular Rosacea.
3. LE: Malar Erythema but no papulopustules.
4. LMDF: lupus Miliaris disseminated Faciei ; (See below)

5. Haber Synd. (See below).

6. Erythematotelangiect. Rosacea → (مع تقدم العمر) Dermatoheliosis.

7. Periorificial Dermatitis → Perioral ECZ. / Periorbital ECZ.

- Haber Synd:
  - AD condition, some times overlap ē Dowling-Degos
  - C/P:
    - Early life: Persistent Rosacea like facial Eruption.
      ± Comedones & pitted atrophy.
    - Later on: Keratotic Follicular Papules on Trunk & Extremities.

"FIGURE"

Lupus Miliaris Disseminatus Faciei (LMDF)
(Acne agminata) = Acnitis.

Def.: an uncommon, chronic, inflammatory dermatosis characterized by red-to-yellow or yellow-brown papules of the central face, particularly on and around the eyelids.

Etiology and pathophysiology: Uknown but may be due to . Reaction

1-Tuberculid reaction to MYCOBACT.-TB.

2-reaction to Demodex folliculorum.

3- granulomatous reaction to hair follicle destruction or ruptured epidermal cysts.

Epidemiology: more in asian Young males(20th). (♂>♀)

C/P: Lupus miliaris disseminatus faciei (LMDF) manifests red, brown, or yellow-brown papules that appear singly or in crops. The papules appear on the central face, especially on and around the eyelids of young adults. They are found predominantly on the face in areas traditionally affected by rosacea.

Lesions occasionally may be generalized and appear on the extremities or trunk. Axillary lesions may be mistaken for antiperspirant-related granulomas. Lesions may present later as crusts, pustules, and, ultimately, scars. → Pitted (Pox like) Scars.

Pathology:

Early: lupus miliaris disseminatus faciei (LMDF) lesions show superficial perivascular and periappendigeal lymphocytic infiltrates with a few histiocytes and neutrophils.

Fully developed lesions: show round granulomas, often with caseation necrosis.6 The changes mimic miliary tuberculosis. Mixtures of sarcoidal and tuberculoid granulomas also may be seen. Late lesions show fibrosis with scattered lymphocytes, histiocytes, and neutrophils and also may be perifollicular and may show epidermal thinning.

(i) Early:
(ii) Fully developed:
(iii) Late: Fibrosis

Tuberculoid like.

TTT:

(1) Medical: A variety of medical treatments reportedly are effective in lupus miliaris disseminatus faciei (LMDF), although controlled studies that support one treatment or group treatments as optimal are lacking. Reported therapies include the following:
Low-dose prednisone, Intramuscular triamcinolone, Dapsone, Tetracycline products
Antimalarials, Pyridoxine hydrochloride, Riboflavin, Isotretinoin

(2) Surgical: * Scar revision procedures.
* 1450-nm diode laser and Pulse-dye laser.

NB - Demodex Folliculitis: Rosacea like facial Erupt. may occurs in Immuno Compromised patients (HIV & leukemia). # → ??